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DISEASE OF MIND AND DISORDER OF BRAIN*

BY

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The centenary of the foundation of the National Hospital, Queen Square, is a fitting occasion for the praise of famous men, and it is opportune that the Sir William Gowers Memorial Lecture falls due to be delivered at this time. My predecessor in this task drew for us, in his brilliant and inimitable style, a picture of Gowers better than any I could present to you, and pointed the contrast between Gowers and Hughlings Jackson, the naturalist and the philosopher (Walshe, 1956). It is to the fortunate association in the early days of the Hospital of two men of genius so different in their outlook, yet alike in their aims, that we owe in large measure the tradition which has inspired their successors to this day. It is difficult to know which has had the greater influence, for their interests were complementary and combined to form a discipline of clinical neurology at a scientific level far higher than that generally obtaining in medicine at that time. Jackson's has been the greater fame. We have, perhaps, taken too much for granted what we owe to Gowers, both for his own minute and accurate descriptions of disease and the methods of observation he developed and enjoined upon others. If in this lecture I refer to Jackson as often as to Gowers it is because their contributions to my subject were of equal importance and closely linked.

The Biochemical Lesion

Gowers's greatest interest was in the patterns of nervous disorder and their classification. He sought especially for symptoms and signs that could be related to structural lesions and was convinced that in diseases such as paralysis agitans more refined methods of observation would show structural damage at the time unseen. He did not, however, believe that the microscope would necessarily reveal such lesions even in the most severe interruption of neural function if this were reversible. Thus he was impressed by the failure to discover any histological abnormality in fatal cases of acute ascending paralysis of the Landry type, and by his observation of occasional rapid recovery from the illness. The interpretation he put forward was that the paralysis was due to some toxic influence acting upon "the ramification . . . in which the pyramidal fibres must end in the grey matter and by which they are connected with the lower segment" (Gowers, 1886). He adduced, as an example of the kind of effect he had in mind, the abolition of the function of nerve-endings in muscle by curare. This is an instance of his ability, from his wide knowledge of medicine and its physiological background, to give whatever speculation in which he might indulge a foundation in fact. He envisaged what we should to-day call a biochemical lesion.

Many other examples might be quoted of his power of deducing a principle from clinical observation and following it through to its logical conclusion. In discussing the selective, symmetrical incidence of lead palsy, after rejecting other hypotheses he says:

> "It can alone be due to some slight inherent difference in the minute constitution of the nerves which enables the atoms of lead to join with the atoms and molecules of these nerves and derange the process of their nutrition, acting on these nerve fibres and not on others. . . When we think of the fact how great is its significance. Those nerve fibres, for some reason, have not the power of resistance to a morbid chemical agent as other nerves have. They differ in their behaviour when a molecule of a metallic poison is presented to them, although they are the same in the minutest scrutiny we can give them, the same to every other test we can apply. . . The various effects of different poisons bring before us in almost startling clearness how profound is the influence of differences far beyond our powers of scrutiny." (Gowers, 1895.)

Evidence for a Physical Basis

Gowers was also an ardent collector of cases in which the phenomena of nervous disorder were mainly or wholly subjective but presented features sufficiently distinct to be clearly recognizable in a group of such cases. This for him was convincing evidence of a physical, as opposed to a psychogenic, basis. Nowhere is this conviction more clearly expressed than in his comment on the subjective phenomena of what he called the vaso-vagal attack. "To dismiss it," he says, "as a hysterical fancy is simply to push it out of sight with the foot. So definite a feeling must have a definite origin" (Gowers, 1907).

His insistence on the rule that symptoms should not be regarded as hysterical because they are strange led him to many valuable conclusions, some of which are still neglected. His description of what he called encephalic vertigo as an occasional occurrence in labyrinthine disease could not be clearer. "It differs from the ordinary sensation of subjective vertigo in seeming to be within the skull, not to involve the head as a whole. The brain seems to the sufferer to be turning over and over or round and round. . . . It is not only strange in character but peculiarly distressing."

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(Gowers, 1907.) He presents illustrative cases. Yet half a century later patients with this symptom are often diagnosed as hysterical simply because it is so strange.

In common with other writers of his time, Gowers observed a distinction between organic and functional nervous diseases. He was careful, however, to define what he meant by these terms. "The term organic disease," he writes in the introduction to his textbook, "as commonly used means visible disease. But visibility is partly relative: it depends upon the means of vision." He goes on to remark upon the use of the microscope and the development of staining methods which have rendered visible changes that could not before be seen, but adds: "Molecular changes in nutrition, considered as such, must be colossal to be detected. Such alterations not sufficient to be seen probably constitute the morbid process in many diseases that are commonly regarded as functional. Hence we may distinguish a class of 'nutritional disease' from those that consist in a mere derangement of function. While distinguishing these two classes we cannot entirely separate them, because nutrition and function are mutually dependent, and prolonged functional disturbances may determine nutritional change."

Gowers wrote little about mental disorder. It almost seems as if he found the subject distasteful. In discussing the mental symptoms of organic disease of the brain he writes: "With the much disputed relation of mind to brain the physician has nothing to do" (Gowers, 1886). Nevertheless, some of his observations and conclusions—the validity of subjective symptoms as evidence of a physical cause, the selective action of poisons upon a group of apparently identical neurones, and the concept of the invisible lesion—have an important bearing upon the psychological symptoms of functional nervous disorder.

Examples of Psychical Disorder

Jackson wrote much about psychological disorder and repeatedly insisted upon the distinction between psychical and physical phenomena, but applied to both his concept of dissolution as a process which as the result of a loss of function permitted the appearance of positive symptoms representing the action of the healthy parts remaining. The simplest example of this kind illustrating psychical disorder is agnosia, and it is in the most restricted forms of agnosia that there is greatest opportunity for observation. Such cases are rare, and this must be my justification for recalling one that I have previously recorded. The patient was a soldier aged 21, intelligent, quiet, and reserved. As the result of a very small penetrating gunshot wound in the occipital region he lost the perception of distance without any other disability. The evidence for this is to be found in the report to which I have alluded (Symonds, 1945).

This young man, who came under our observation a fortnight after his injury, was then ambulant and active. He made no complaint of anything wrong, but peculiarities in his behaviour attracted attention. He was disinclined to move about, and, when he did so, progressed in a slow, hesitant manner. When he walked along a corridor in which there was a corner he approached the wall facing him with his arms outstretched, turning only when he felt it. He was examined by several experienced observers, who concluded that his behaviour was hysterical. It is to the credit of Dr. Charles Phillips that he first suggested the true explanation, but this at first was doubted because of curious discrepancies. When the patient was asked to estimate the distance of a wall opposite to him in the empty room in which he was examined he could not do so. But when he stood at one end of his ward and was asked to judge the length of it he did so, after an odd pause, with fair accuracy. The explanation, when provided by himself, was simple. He knew roughly what was the usual width of a bed and the distance between beds, and by multiplying this by the number of beds had arrived at his estimate. There were many other instances of this kind of behaviour.

I have related this case as an example of psychological disorder which at first, because it was so peculiar, was thought to be hysterical, but in fact represented the attempt of the mind to work when deprived of one of its tools. I submit that psychological disorder of much greater complexity deserves examination from this point of view.

In the case mentioned there was a demonstrable relation between local brain damage and psychical symptoms. The next group of cases to be considered is that in which there are psychical symptoms of a particular kind associated with evidence of organic disease of the brain, but with no demonstrable localization. Of the many possible examples I shall take two. The first is that of encephalitis, leaving in its wake a very distinct pattern of intellectual impairment comprising a persistent retrograde amnesia covering several years, and gross defect of recent memory with little interference with other intellectual functions. Immediate retention is unimpaired, and skills and knowledge acquired before the illness are preserved. The patient is therefore able to achieve a good score on intelligence tests, failing only on those requiring recent memory. He is able, for example, to retain eight digits, do serial subtractions and similar tasks quite well, and yet fails to remember any item of a name, address, and flower given to him five minutes previously. Recognition is affected as well as recall, and learning of new material is impossible. Comparable symptoms have been observed after bilateral temporal lobe resection.

Of equal interest is the defect of moral sense resulting in children from encephalitis lethargica. Many examples were recorded at the time of the epidemic without recognizable impairment of intellectual function, and sometimes without any of the physical sequelae commonly observed after the illness. There can be no doubt of the organic basis of the defect, which is usually irreversible, though we have no clues in this instance for localization. What is most remarkable is that this sequel did not occur in adults, suggesting that whatever structures are involved are essential for learning to distinguish between right and wrong but not necessary for the preservation of such distinction, or, to put it in another way, if learning has continued long enough the process involved has produced physical changes in such a widespread net of neurones that local damage has not the same effect as it would have at an earlier stage of the process. Whatever the interpretation may be, we seem to be dealing with a kind of moral agnosia, and observe the mind deprived of this sense proceeding to the most ruthless extremes of antisocial conduct. In this there is reasoned direction, and often great skill in escaping detection and punishment. Granted the defect, thought, feeling, and behaviour are rational.

Functional Psychoses

We now come to the much larger category of psychical disorders in which there is no direct evidence of cerebral disease, of which the most important are the functional psychoses. Before embarking on this subject I shall refer to what Jackson had to say upon it in his essay on "The Factors of Insanities" (Jackson, 1894).

> "In every insanity more or less of the highest cerebral centres is out of function, temporarily or permanently, from some pathological process; for my present limited purpose it matters little what that process may be. It only matters as the pathological processes produce loss of function, that is dissolution, of more or less of the highest centres. I do not use the term function in the sense often given to it in clinical accounts of nervous maladies, as, for example, when it is said of a patient that 'his case is entirely functional.' I do not believe that there is such a thing as loss or defect of function of any nervous elements without a proportionate material alteration of their structure and nutrition. Of course the separation into structure, nutrition and function of the nervous system is artificial; it is merely a convenient device, just as the separation into the surface, weight and mass of a body is."

He then goes on to enumerate what he calls the four factors of insanities as they may be applied to the confusion and allied conditions in terms of his theory of dissolution, and continues thus:

> "Although I speak of dissolution of the highest cerebral centres as if it were uniform—as if all the divisions of these centres were 'evenly' affected—it is clear enough that there are local dissolutions of those centres. That there are different *kinds* as well as different *degrees* of insanity is evident—melancholia and general paralysis for two examples. Different regions of the highest cerebral centres undergo dissolution in different *kinds* of insanity."

He ends his essay with the surmise that the causes of certain of the insanities may be found to lie not within the brain itself, but in the organs which supply its nourishment.

Although their approach is different we find little divergence between the conclusions arrived at by Gowers and by Jackson about what is meant by functional nervous disorder. Jackson, however, went much farther along the road that leads from neurology towards psychiatry. It is, I think, natural that he should have taken melancholia as one of his examples of local dissolution, for the clinical pattern of this illness in its severe forms is remarkably constant and distinct. "So definite a feeling must have a definite origin." Gowers's dictum is all the more applicable if the psychosis is regarded not only as a disorder of mood but a disorder of feeling which will account for the great variety of dysaesthesiae that may be observed in the illness—head discomforts, general malaise, bodily aching, and disturbance of visceral feeling, for example. In the milder degrees of the illness it is of symptoms of this kind that the patient may chiefly complain. The increasing recognition of these milder degrees and of their great frequency has led to difficulties in terminology, which have not yet been solved. Those patients who are mildly affected are obviously not insane, yet the illness is often called psychotic so that the affective disorder may be distinguished from that which is termed neurotic.

Affective and Schizophrenic Illness

Concerning the distinction between endogenous and reactive forms of depressive illness I will say nothing except that I am doubtful of its validity. It will suffice for my present argument if it is admitted that there are many cases both of the severe and of the mild degree in which the onset is without discoverable cause, physical or psychogenic. They are endogenous so far as we can see. I would like to add, however, that this is equally true of some cases in which the disorder of affect is not depression but fear; for these patients, because they are anxious instead of depressed and because anxiety is a pure form is not generally accepted as a characteristic of endogenous affective disorder, are often regarded as suffering from a neurosis.

The arguments for supporting Jackson's assumption that this disease of mind represents a regional disorder of function in the brain are many. We may first consider the evidence in favour of believing that the illness has a physical basis irrespective of localization. Some of the arguments are equally applicable to the other functional psychosis—schizophrenia, and I will take first those observations which are relevant to both diseases. The absence of psychogenic cause is notable, though it must be regarded critically owing to the possibility of emotional stress which the subject is concealing or of which he is unaware. Much has been made of unconscious emotional disorder in the aetiology of the psychoses, especially by the psychoanalytic school. Demonstrable proof of this is lacking, and it is, I think, fair to assume that the patient who complains that he feels sad although he has a satisfactory job, a good wife, and a comfortable home, and believes that he has no reason whatever for unhappiness, is usually speaking the truth. The illness is as much a foreign body as he thinks. In the schizophrenic it is harder to estimate psychogenic factors in the aetiology owing to his thought disorder; but again, when all the facts are considered, psychogenesis is conspicuously absent in most cases. The distinct clinical pattern of the illness has already been mentioned. It is again more readily observed in the affective disorder than in schizophrenia, but of either illness it may be said that the symptoms have as much validity for the experienced clinician as those of a duodenal ulcer or angina.

The strongest evidence, however, for a physical basis is the genetic factor as demonstrated especially by the study of uniovular twins. In Kallmann's (1953) series the percentage of twin partners similarly affected by manic-depressive psychosis was for uniovular twins 96% and for binovular twins 25%; in the case of schizophrenia the concordance for uniovular twins was 86% and for binovular twins 15%. Slater's figures for concordance in a similar investigation of the affective disorder, analysed by Fonseca (1959), were in uniovular twins 75%, in binovular twins 38%. These figures compare with an expected incidence for the general population of 0.4% for manic-depressive psychosis and 0.8% for schizophrenia.

Spontaneous recovery from an episode of manic-depressive illness—as much endogenous as the onset—is further evidence for a reversible physical disorder. Moreover, the response of depressive illness to electric convulsion therapy, mysterious though it be, is clearly a physical effect. On the other side, it must be observed that in neither the affective disorder nor in schizophrenia has there been any histological proof of cerebral disease,

with the possible exception in schizophrenia of the dwarf cells in the thalamus found by the Vogts. In the affective disorder one might accept without difficulty the absence of histological change; for the illness, however severe and of whatever duration, may be reversible. I have myself observed recovery from a certifiable depressive illness of ten years' duration in a woman at that time aged 60. Once improvement began recovery was complete in a few weeks. This was before the advent of E.C.T. In schizophrenia histological lesions are more to be expected. Perhaps they may yet be seen. It is not yet certain that the lesions responsible for paralysis have been identified. On the other hand, the lesion, though irreversible, may be biochemical, without visible change, as Gowers surmised might be true of many functional disorders.

We have to conclude that in neither of the functional psychoses is there proof of organic cerebral disease or even of selective biochemical disorder. The evidence for their physical basis is strong but circumstantial. It is nevertheless worth pursuing the inquiry further and asking what evidence may be found for supposing that if a physical basis does exist it is of a focal or regional kind. I use these terms not in a morphological sense, but to indicate the possibility that particular systems of neurones may be involved. Here again the distinctness of the clinical pattern may be put forward as a reason for supposing that in each of the diseases under consideration particular, and different, neurophysiological dispositions are involved. Further evidence has become available in recent years from the use of drugs.

Specific Patterns Produced by Drugs

One of the most interesting experiences for neurologists of my own generation was the appearance of Parkinsonism and other stereotyped motor phenomena after encephalitis lethargica. Here was an example, comparable with that of a lead palsy, of a remarkable selective action upon particular units of the central nervous system by a new neurotropic virus. Equally remarkable has been the experience in recent years of witnessing identical symptoms, including the oculogyric crisis, after the administration of new drugs (Heaton-Ward, Carpenter, and Jancac, 1959). We may conclude that the disease and the drug have each affected the same region, and this observation is likewise relevant to the effect of drugs in causing specific patterns of psychical disorder.

For some years it had been noted that mescaline would produce in normal subjects psychological disorder in some respects resembling that of schizophrenia. It was by chance, however, that Hofman, in 1943, in the pursuit of chemical experiments with L.S.D.25, discovered in himself remarkable effects, which he subsequently proved to be reproducible by the ingestion of minute quantities of this drug. Out of this work has evolved a considerable literature dealing with the resemblance of the psychological disorder thus produced to that of schizophrenia. The hallucinations, thought disorder, and disturbance of affect and behaviour have been regarded by many as representing a model of schizophrenic psychosis, but critical consideration of the published data makes this doubtful. The fact remains, however, that L.S.D.25 can cause psychological disorder of a very complex and fairly constant pattern. Whether the experimental psychosis exactly resembles schizophrenia or not, the experiment has shown that a psychosis of this type can be produced by the action of a particular chemical substance, which may be presumed to act upon a particular region of the brain.

It is also worthy of remark that certain drugs, of which imipramine is the current example, can have a specific action in relieving depressive illness. On the other side, it has been learned by chance that *Rauwolfia serpentina* prescribed for arterial hypertension may sometimes cause an illness hardly distinguishable from a depressive psychosis.

Manifestations of Epilepsy

Epilepsy, as Jackson was the first to observe, provides an opportunity of studying psychological symptoms of varied and distinct patterns, and establishing some degree of correspondence of the pattern with the region of the brain involved in the epileptic discharge. Owing largely to the work of Penfield and his collaborators, a considerable body of data has been accumulated on this subject. I shall first consider those observations that are relevant to endogenous effective disorder. They have been studied in detail by Denis Williams (1956). That a paroxysmal disorder of mood may occur as a manifestation of epilepsy was recognized by Jackson and has repeatedly been observed since, and it is generally agreed that fear is the most frequent experience. This is commonly described by the sufferer as irrational and without relation to any relevant thought or memory. The patient tells us simply that he is intensely frightened of he knows not what. He recognizes the emotion as unnatural. He may even say that it seems to be coming from inside him. The subjective experience, except for its brevity, seems identical with that of the patient with an endogenous fear state, who complains of a state of fear and foreboding for which there is no cause.

Ictal depression is less often met with, but again, apart from its duration, is indistinguishable from the descriptions given by patients with affective disorder. The experience described may be simply a feeling of intense sadness or may have some reference as in the case of a boy aged 13 whose minor attacks were preceded by a feeling which he described as "like a guilty conscience as if you'd murdered someone or stolen something," At the same time he had an epigastric aura. His head then turned to the left and he lost his senses for a few seconds. As he came to himself he would sometimes wonder what he had stolen or whom he had killed.

The resemblance between forced thinking and hallucinatory experience occurring as ictal phenomena, and similar subjective symptoms in schizophrenia, has been the subject of an important paper by Karagulla and Robertson (1955), who record the various graduations from amorphous thoughts to auditory or visual hallucinations observed in temporal-lobe seizures. They have stressed the difficulty patients have in describing such experiences. My own observations include several of a schizophrenic character. Of particular interest are ideas of reference and passivity. One of my patients, if at the onset of a minor seizure she was in conversation, felt that the other person was repeating what was in her own mind. Another described "something directing me to do something I don't want to do. It may be something about the house I'm going to do. My mind somehow tells me not to do it." In another case the warning of a major seizure was of voices rapidly repeating, "Yes, you did, No, you didn't," etc., for a second or two. As Kinnier-Wilson (1927–8) observed, epilepsy cannot call into being physiological processes

that do not exist. It may be argued, therefore, that the psychical symptoms which have been described are dependent upon the isolated and therefore distorted evocation of functions regionally represented.

Of further interest in relation to schizophrenia is the occurrence of chronic mental disorder in epileptics resembling very closely the ordinary schizophrenic psychosis. Mayer-Gross, Slater, and Roth (1960) have observed feelings of passivity with ideas of reference, paranoid moods, hallucinations, and catatonic phenomena. They conclude that the close clinical similarity to schizophrenic symptomatology must be significant and is more likely to be accounted for by a like regional site than by any common factor in the pathology.

Association of Schizophrenia with Cerebral Tumour

If the symptoms of schizophrenia are the result of disordered function in a particular region of the brain it might be expected that they would occasionally result from coarse disease—for example, a tumour. Such an occurrence might be exceedingly rare, for it would be essential for the appearance of such symptoms not only that certain functions should be put out of action, but that other functions should remain in action, and in the hypothetical case it is probable that the anatomical substrata of these functions are closely related. The coarse lesion is not selective enough; it destroys too much. For the same reasons one would expect, in the case of a growth, that if such symptoms occurred they might be of transient duration, disappearing as the destruction increased. This sequence I have observed in a few cases of cerebral tumour. The occurrence is so rare that it has been dismissed as coincidence. Yet the sudden appearance at the same time of the symptoms of tumour and schizophrenia is sometimes impressive.

In one of my cases there was further evidence of a very suggestive nature. This patient was a man aged 35, a scientific worker of high intelligence, with no previous evidence of mental abnormality, who in the fortnight before his admission to hospital had had several attacks of an epileptic character. During this period he had also developed symptoms which, on admission, were indistinguishable from those of a schizophrenic psychosis. He showed the incongruity of thought and affect, thought disorder, and bizarre delusional ideas characteristic of the condition without, so far as could be judged, any clouding of consciousness. Subsequently he became drowsy, with signs suggesting a left frontal tumour, and died a fortnight after his admission to hospital after ventriculography and biopsy. At the necropsy a tumour was found involving the corpus callosum and extending forward into the left frontal lobe. Histologically this was a glioblastoma.

Two years previously this patient's sister, then aged 34, had come under the care of Dr. Hugh Garland on account of occasional epileptic seizures. She was a school-teacher with no mental abnormality. In the course of time physical signs developed, leading to the diagnosis of a left posterior frontal tumour, and five years after the first symptom an exploratory craniotomy by Mr. W. R. Henderson revealed an infiltrating glioma in this situation. Histologically this was an oligodendroglioma. After the operation she rapidly developed symptoms of mental disorder and was transferred to a mental hospital, from which, through the courtesy of Dr. R. W. Bryson, I have been able to obtain particulars. These I need not describe in detail. They were typical of a schizophrenic psychosis.

It is a remarkable coincidence that brother and sister should both have had a cerebral tumour and that in each case the same area should have been involved. The tumours were of different histological types, and, in any case, evidence of a familial incidence of cerebral gliomas, apart from those that may occur in neurofibromatosis, is, so far as I am aware, lacking. Probably, therefore, we must accept coincidence thus far. But it is difficult to accept further coincidence as the explanation of the schizophrenic psychosis in both cases. In this direction it is natural to look for a genetic factor, having regard to the observation that if one sibling has schizophrenia the chance of another being similarly affected is 14% as compared with the incidence of 0.8% for the whole population. We may then argue that the genetic factor somehow operated in determining the pattern of mental activity in what Jackson called the healthy parts remaining after the destructive lesion. If so, was the site of the destructive process, similar in the two cases, significant? We cannot be sure that it was, for account must be taken of epileptic activity in the brains of both patients, and of the possibility of diffuse interference with cerebral function by increased intracranial pressure. The question of regional significance should, however, be pursued further. A study of the incidence of schizophrenic symptoms in patients who have had gunshot wounds of the brain might possibly yield information.

Conclusions

Examples have been given of specific patterns of psychological disturbance caused by organic cerebral damage. Evidence has been presented which suggests that the two diseases of mind which we call affective and schizophrenic are the effects of functional disorder in the brain, and that each represents what Jackson called a local dissolution, the region being different in the two cases. Neurologists hitherto have not taken much part in the investigation of these conditions, partly because they have been busy with other problems, partly for lack of opportunity. The opportunity has fortunately been provided at the National Hospital by the establishment of a psychiatric unit, which, it is to be hoped, will in due course expand. Jackson saw no more incongruity in classing together progressive muscular atrophy and insanity, upon the basis for advancing scientific knowledge, than in the botanist's classification of the bamboo with common grass. If he was right, neurology has a duty to contribute its share towards the understanding of these diseases of mind which fill more hospital beds than all other nervous disorders combined.

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JACKSONIAN IDEAS AND THE FUTURE, WITH SPECIAL REFERENCE TO APHASIA*

BY

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The hundred years which have passed since the modest beginnings of the National Hospital have witnessed the emergence of neurology as an independent discipline, the offspring of general medicine and of physiology.

The art and thinking of clinical neurologists in Great Britain to-day stem directly from the teaching of pioneers whom few among us here ever saw. To our cradle of neurology they brought priceless gifts. Here I would like to focus attention upon one of these giants—namely, Hughlings Jackson—to discuss Jacksonian doctrines in their formation, their present status, and their promise for the future, especially in the realm of language.

In this country we often refer to Jacksonian ideas and methods in clinical medicine. We all like to believe that, consciously or unconsciously, we are incorporating his particular mental attitudes into our own workaday practice. By and large, all of us endeavour to emulate his tenets and his methods, even though many of us fail to live up to his model.

Just what is understood by Jacksonian ideas? To unravel the golden threads which run through the texture of his obscure writing is no easy task, but it is a rewarding one.

Observation and Replication

In the first place we owe to Jackson our realization of the need for exactitude in observation coupled with faithfulness in recording. These principles, seemingly banal, are sometimes forgotten. As an observer, Jackson was shrewd, patient, and painstaking. Witness his retracing of the march of a local seizure by dint of untiring study and reportage of fit after fit. Some of this research was tinged with tragedy, as when his beloved wife herself fell a victim to Jacksonian epilepsy. To the acuity of his gaze was added the utter honesty of his documentation. He stressed the necessity for describing exactly what the patient did or said; and he pointed out the dangers of rationalizing or interpreting, which might lead to an inaccurate note that would merely record what the observer deemed should have taken place.

An example may be given. In an early paper, written when he was 29 years of age, Jackson commented on the common failure of a patient to protrude the tongue on request. Asserting that we do no harm to clinical medicine if we simply record all the facts, he stated that the patient when asked to put out the tongue betrayed that he understood the request by putting his fingers into his mouth as if to help it out; and yet nothing would happen. Such would be a true statement of facts, giving the reader a basis from which to speculate. To say "there is total paralysis of the tongue" would be to advance a theory, improbable on the face of it, and, if wrong, all the more dangerous since it might even pass for a fact. That the tongue actually is not paralysed is revealed by the patient's ability to chew and to swallow. He may lick his lips. As the daughter of one of his patients remarked, her father could protrude the tongue "by accident" as it were. Jackson saw in this paradox a performance reduced to a more automatic condition.

The second splendour of Jackson's neurology lay in his reflective cast of mind. Mere noting of data was not enough. Always he was asking himself "Why?" This imagination, restrained and disciplined, led to creative and original thinking, and marked him out from the company of his talented colleagues. Jackson owed this gift of vision to his philosophic bent, for it had been his early ambition to devote himself to philosophy. A devoted disciple of Herbert Spencer, he was rescued for medicine largely by the encouragement of Jonathan Hutchinson.

An Era of New Ideas

The mid-Victorian period was an era of exciting new ideas that naturally conduced to Spencerian thinking, and thence to Jacksonian hypotheses. Anticipated to some extent by Linnaeus, Buffon, Erasmus Darwin, and Lamarck, the doctrine of evolution came to life in the writings of Russell Wallace and of Charles Darwin. When the *Origin of Species* was first published Spencer was 39 years of age and Jackson was 24. Every branch of science became profoundly influenced in one direction or another by the impact of these stimulating notions.

It is unlikely that Jackson ever met Spencer personally. They corresponded, however, and Jackson sent Spencer a reprint of one of his articles on dissolution within the nervous system. The philosopher was impressed, describing the paper as "clearly and conclusively argued." Spencer had first mooted his evolutionary ideas in his essay in the "Development Hypotheses" (1852), being himself considerably influenced by the "congruous formula" of the zoologist K. E. von Baer, or development from the homogeneous to the heterogeneous. In the "Art of Education" (1854) the proposition was developed that the unfolding of a child's mind repeats the unfolding of the mind of the human race. Spencerian notions reached fruition, so far as Jackson was concerned, in the *Principles of Psychology* (1855).† Spencer had said that progress in mental as in nervous organization is presentable in terms of evolution (and we may interpolate here that it was Spencer who first used the term "evolution"), for in rising to the higher types of mental states characterized by definiteness, coherence, and revivability, progress takes place in integration and heterogeneity.

Jackson's Stages in Motor Evolution

Jackson paraphrased Spencer, and isolated four stages in motor evolution—namely, (1) increasing differentiation (that is, greater complexity); (2) increasing specialization (that is, greater definiteness); (3) increasing integration (that is, greater width of representation); and (4) increasing co-operation (that is, greater association).

Jackson borrowed from Spencer the term "dissolution" to signify the opposite of evolution. By applying

*Centennial Oration of the Institute of Neurology given at County Hall, London, on June 22, 1960.

†When, in 1896, Spencer announced that he contemplated a system of synthetic philosophy, Jackson added his name to the list of guarantors.

it to disease of the nervous system, he explained certain clinical appearances. The conception of evolution and of dissolution in neurology led logically to other bold ideas, such as the notion of levels of function within the nervous system. A contrast between positive and negative manifestations of disease became obvious, and Jackson insisted that positive clinical phenomena could not be directly due to negative lesions. For example, an aphasiac might utter wrong words like "chair" for "table." But while it could be held that softening of the brain was the cause of the distorted speech, it could not have been the cause of wrong utterances. "Softened brain is no brain; so far as function, good or bad, is concerned, it is nothing at all." Wrong utterances occur during activity of healthy parts, not softened. The most that Jackson would concede was that the diseased brain "permitted" wrong words to be used. Jackson would therefore equate positive clinical data with a negative state of the brain only in the legal sense of a *causa causans*, or remote mechanism.

In the same common-sense vein, Jackson stressed the uselessness of medicinal treatment for negative conditions. "What will drugs do towards ridding the patient of his paralysis? Nothing. No drugs can do anything whatever, good or bad, for cerebral softening; softened brain is not brain at all; it is dirt in the brain. . . . He who is treating by drugs hemiplegia owing to softening, or to clot, is treating a hole in the brain."

Another principle formulated by Jackson is often forgotten to-day, though its validity has never been challenged. Jackson stressed the error of trying to localize a cerebral function on the grounds that a focal lesion within the brain was followed by loss of that function. This doctrine was slow in maturation. For example, early in his career Jackson was willing to accept Broca's teaching *in toto*, first regarding the position of the focus in cases of aphasia; and, secondly, that a faculty of language resided within the third frontal gyrus. Later Jackson grew more sceptical. In 1889 he confessed that at one time he had spoken of centres for will, memory, reason, and emotion; he now realized them to be elements of consciousness quite artificially distinguished. To have imagined such centres had been "a mere artifice." He could not now accept any abruptly demarcated centres in the cortex standing for any kind of representation. In another context Jackson admitted that he had now abandoned the words "faculty" and "reside" in the arbitrary manner he had used them in the past. Since speech or words enter into thought, it now seemed to him incredible that "speech" should "reside" in any limited spot. None the less, he believed that *damage* to the brain confined to the region of the corpus striatum would bring about a loss of speech. As Jasper has recently put it, anatomical areas within the brain are not to be rated as anything more than regions which, when ablated, may be followed by disturbances of function. They are to be looked upon as "centres of destruction" rather than centres of function.

Borrowed Terminology

Jackson protested against another example of muddled thinking—namely, the employment within the same context of terminology borrowed from unrelated disciplines—for example, anatomy, metaphysics, and physiology. Thus the word "voluntary" was a psychological term which could not really be used when speaking of physical processes. Classifications which were partly anatomo-physiological and partly psychological obscured the issues. Such confused sorting would be as scientifically improper as would be a grouping of plants into endogens, *graminaceae*, kitchen herbs, ornamental shrubs, and potatoes. He gave as an example of such mixed taxonomies the common statement that an *idea* of a word would produce an articulatory *movement*; whereas, he argued, a psychical state, an "idea of a word" (or simply "a word") could not possibly produce an articulatory movement, which is a physical state. "In all our studies of diseases of the nervous system we must be on our guard against the fallacy that what are physical states in lower centres fine away into psychical states in higher centres."

Like Bergson years later, Jackson was critical of the teaching that verbal memory resided within the brain. There is no such thing as memory, but only things remembered. Dealing in this vein with the common employment of the term metaphysics in a pejorative sense, Jackson declared: "It is a mistake to suppose that those who write books on metaphysics are the most metaphysical. They have, at any rate, the knowledge that they are dealing with metaphysics. There was once a man who could conceive an abstract Lord Mayor. The conception he had, so he averred, had neither head, arms, legs, nor corpulence; it was not an image of any particular Lord Mayor nor a fusion of several, but an abstract Lord Mayor. Well, we think this metaphysician was too confident in his powers of conception. But do we not imagine ourselves capable of the same kind of marvellous feats? Let us look at a case of aphasia. A man does not speak and yet can understand what we say to him, and can think, on ordinary things, at any rate. These are the facts; no one disputes them. Now comes the metaphysician, who proffers an explanation that the patient has lost words, but retains the memory or ideas of words. There are, it seems, words, and also memories or ideas of words, which latter somehow are not words. Now what is an idea of a word which is not a word? It is, like the abstract Lord Mayor, simply nothing at all" (1882).

In the mental processes preceding articulation Jackson recognized a twofold manœuvre. First the mind becomes aroused in propositional form: later comes a fitting of words to the idea. These two stages—namely, subject-proposition and object-proposition—together make up verbalizing. The fitting of words to the idea comprises external speech if it achieves audibility, but if the phase takes place in silence it forms internal speech. Jackson did not believe there was any distinction other than in degree between internal and external speech. The speechless man is not wordless: he can receive propositions: he is not bereft of images. He can think, but he is lame in thinking. But if imperception is added to speechlessness, as is often the case, images will be affected, and there will be inferior comprehension.

Jackson's Early Years

Such were a few of Jackson's ideas relating to language. At this point it might be interesting to pause, and to inquire about the man himself. What were the influences that bore on him and directed the stream of his intellect into the novel discipline of neurology?

John Hughlings Jackson was born in 1835 in a Yorkshire hamlet. He received his schooling first in the village, later still in Tadcaster, and afterwards in a progressive nonconformist school recently opened at

Nailsworth, Gloucestershire. Formal schooling meant but little to Jackson, who always regarded himself—like the Sitwells at Eton—as largely self-taught. All his schools were bad, he said, and much of his later success was due to his not having been overeducated. It is probable that Jackson was never an erudite man or a cognoscente.

At 15 years Jackson became an apprentice to Dr. Anderson of York, where he also joined the local medical school. After qualification he held the post of resident medical officer at the York City Dispensary from 1856 to 1859. There he came in contact with a remarkable physician, Dr. Thomas Laycock, who afterwards occupied the chair of the practice of physic at Edinburgh. Laycock was a scholarly man who had been impressed by the work of Marshall Hall upon nervous reflex action. Jackson was certainly influenced by Laycock, who may well have helped orientate his attention towards the nervous system.

Moving to London in 1859, Jackson lived with his friend Jonathan Hutchinson at No. 4, Finsbury Circus. Thanks to him, Jackson became employed as a fellow reporter for the *Medical Times and Gazette*. Their duties took them to medical meetings and to hospitals, where they selected clinical cases and met the leaders of the medical profession. Among these was that brilliant original, Brown-Séquard, who for a few years was making London his home—the brief sojourn of an unstable eccentric. In 1859 Brown-Séquard had been invited to join J. Z. Ramskill on the staff of the projected National Hospital for the Paralysed and Epileptic, whose first patients were received in the spring of 1860 at No. 24, Queen Square. Friendship with Brown-Séquard determined Jackson's choice of career, and his decision to sublimate his philosophy into the more practical pastures of neurology. When, in 1862, a vacancy occurred at the National Hospital for an assistant physician, Jackson was the successful candidate. Shortly after came further vacancies upon the senior staff. In those days there was no automatic advancement, and it was incumbent upon Jackson formally to apply. Twice in succession he was passed over in favour of others, and it was only when a third vacancy occurred in 1867 that Jackson attained the rank of full physician. It is characteristic of Jackson's easygoing modesty that he wrote that if unsuccessful he would be happy to continue as assistant physician. This makes strange reading when we find him in 1900 seeking to retire from the staff under the age rule, his colleagues, however, persuading him not to do so, but to continue on the active list another 10 years.

Problems of Disordered Speech

From his earliest days in neurology Jackson interested himself in the principles which underlay nervous function in health and in disease. As a corollary he applied his attention to the problems of disordered speech. Here again Brown-Séquard was to prove the instigator. At first Jackson had lightly assigned loss of speech to disease of the olives, a notion which he had derived from Laycock, who in turn had adopted it from van der Kolk. Brown-Séquard, however, showed Jackson that the defect was often not one of talking but of language, and that some of these patients had lost all power of expression, even by way of making signs.

Stirring events had been going on in the medical circles of Paris about the time that Jackson qualified. The opinion of Gall and Spurzheim, so contrary to those of Flourens, had been received with excitement, and there were strong repercussions of sentiment either for or against. Matters came to a head in March, 1861, when Auburtin delivered his thoughtful address on the relationship between loss of speech and lesions of the frontal lobe. Auburtin's role in the history of aphasia has been neglected: many neurologists to-day do not even know his name. And yet it was he who prompted the surgeon Broca—like himself an amateur anthropologist—to observe with particular interest the case of the speechless patient Laborgne, lately transferred to his care by reason of a septic leg. Hitherto Broca had not been concerned with problems of speech. Fortune ordained that Broca's patient should quickly perish, and that the brain should offer up the eloquent evidence of a superficial lesion of the frontal lobe. All these happenings were topical and familiar to young Jackson, who a few years later was to meet Broca personally at a symposium in Norwich. Jackson had also heard about Broca's second patient, Lelong. He was aware of Trousseau's classic demonstration of speechless patients. He had known him reject in succession the terms "aphrasia," "alalia," "alogia," and "aphemia," and substitute them with the now traditional "aphasia." Jackson, be it noted, used none of these terms in his earlier writings, prefering to speak of "disorders of expression."

Jackson must also have read about the curious intervention of Dr. Gustave Dax, nettled at the fancied slighting by Broca of his late father, who had long realized the greater importance of the left hemisphere in the genesis of aphasia.

Jackson's Interest in Aphasia

These events were like heady wine to the young neurologist, who at Queen Square and elsewhere was now in touch with numerous hemiplegics, many with disorders of expression. One of Jackson's duties as an assistant physician was to visit patients in their own homes. In the drab houses within the mean streets of Holborn, Soho, and St. Pancras, bedridden survivors of an apoplexy became a cornucopia of ideas which fed Jackson's inspiration. His colleagues Brown-Séquard and Victor Bazire had collected many such disabled folk and had permitted Jackson to observe them.

But Jackson's interest in aphasia had been whetted long before he met Brown-Séquard. Boyhood impressions are often so deeply etched that they may determine the careers and vocation of later life. So it was with Jackson. When quite a child on a seaside holiday, he lodged at a house where the landlady—as he discovered to his wonderment and awe—could say nothing but "watty." This unlikely disyllable was articulated with such a wide range of cadence that it could express a variety of emotions. Her laugh was merry and ringing, and when anything amused her she would say: "Watty, watty, watty." Years later we find Jackson making the pioneer descriptions of what he was to call the recurrent utterance of aphasiacs.

A little older, he was driving to school, when his fellow-passenger, a girl of 17, daughter of the coachman, suddenly found she could not reply to a question which was put to her. With great difficulty she got out the words: "I can't talk!" The coach turned back, and Jackson afterwards learned that the girl lost speech altogether for three weeks and became paralysed down the right side. Eventually she improved, but she died

12 years later from eclampsia. She never regained her power of speech completely, and even to the last was apt to call things by wrong names.

These two cases encountered early, in intimate even dramatic circumstances, must surely have stamped an indelible imprint upon his eager intellect, which was to influence the direction of his life's work.

Contemporary Neurologists

Ideas, whether they be true or false, have stupendous potentialities in human affairs. But ideas catch on slowly, as Jackson himself used to remark, especially in medicine, where an innate conservation obtains. The second half of the nineteenth century was a period in neurology when clinicopathological correlation was winning easy prizes. The work was descriptive in character, not reflective. It was self-evident and easy to comprehend. Much of it was worthy factual bricks-and-mortar stuff. Little wonder Jackson's ideas, especially an aphasia, were temporarily overshadowed by those who made brief clinical studies highlighting the obvious, and who sought by way of morbid anatomy a key to the understanding of the normal faculty of language.

But the seeds had fallen, and in due course they germinated. Other philosophically minded neurologists appeared whose contributions to aphasia, not necessarily deriving from Hughlings Jackson, nevertheless stand alongside Jacksonian ideas in sympathetic comity. We recall the names of Baillarger, Kussmaul, Pick, von Monakow, Freud, and particularly Bergson. The observations of the last-named upon the topic of language have been surprisingly overlooked. Bringing the story into the early twentieth century, we have Pierre Marie, van Woekoem, Goldstein, Weisenberg, and, most significant of all, Henry Head. Of contemporary English-speaking neurologists, we may enumerate Walshe, Russell Brain, and Walter Riese among the most important exponents of Jacksonian ideas.

To-day, forces of neurology are arrayed differently. By far and away the majority of worth-while research work into aphasia is of a dynamic quality, and harks back directly to Jackson's ideas, offering abundant promise for the future.

New Tools for Research in Aphasia

But the mill will not grind with the water that's passed. Let us rather project our imaginations and speculate upon how aphasiology may be expected to develop in the hundred years ahead.

Already we possess important new tools for research. In the first place, we have the advantage of exact *instrumental methods for the study of aphasic utterance.* Now, under scientifically controlled test-circumstances the fragmentary speech can be faithfully recorded: played back as required, at slower or higher speeds if necessary. In this way the clinician no longer has to rely merely upon his sharp ear to interpret the distorted mumblings of the aphasiac. The clues are now caught and preserved, and they can be transcribed and examined over and over again. The utterances can be analysed from the standpoints of phonetics, syntax, and semantics. The recordings can, if required, be translated from acoustic into visual forms by way of spectography or some other technique of visible speech. Modern aphasiology is consequently furnished with evidence which is scientifically acceptable, and which can be utilized for future research.

Secondly, there now exist *more satisfactory psychological testing procedures,* including the evaluation of non-verbal performance in aphasiacs.

The third asset is a momentous one. A *link-up has taken place between academic linguists and aphasiologists.* To-day, aphasia must be regarded as a problem lying within the province of linguistics. Language in dissolution is obviously an integral part of this stupendous topic, which no neurologist can henceforth afford to neglect. Neither can he longer avoid coming to grips with the essential nature and the purpose of the normal faculty of language. Information theorists overstress the role of communication. Of the many available definitions of language perhaps the most satisfying is that promulgated by Sapir, who said that language is primarily a vocal actualization of the tendency to see realities symbolically, a quality which renders it a fit instrument for communication; in the actual give-and-take of social intercourse it has been complicated and refined into the form which it is known to-day. "Language is a great force of socialization, probably the greatest that exists." Nowadays linguistics forms a broad spectrum of endeavour ranging from philosophy at one extreme to phonetics and communication theory at the other. Here, then, is a vast unexplored territory for the future. Ideas for research crop up in profusion.

Among the present-time neurologists alive to the importance of linguistics in aphasia are Grewel, Bay, Panse, and Leischner. On the other hand, linguists have been rather remiss at recognizing the value of the lessons of aphasia, and such meagre references as they have made are usually quite out of touch with contemporary neurological thought. Ramon Jakobson is a conspicuous exception.

Communication theory includes a statistical study of language. Measurement of vocabulary and frequency of usage of individual words and clusters of words has already been undertaken by Zipf, by Estoup, by Mandelbrot, and by Herdang. It remains for future neurologists to apply these techniques to the writings and utterances of aphasiacs. A similar inquiry into the ratio between the number of different words chosen and the total sum of words employed is likely to be revealing. This is the type/token ratio, which clearly demonstrates that the aphasiac utilizes a very shrunken store of words, while indulging in undue or unnoticed iteration.

The subtopic of contrastive linguistics emphasizes important relationships between the syntax of a particular language and the thought-processes of those that use the language. That the association is integral is the basis of Whorpf's principle of linguistic relativity. Hitherto the great bulk of research into aphasia has been carried out on patients speaking one of the European tongues. Little or nothing is known of the pattern of aphasic dissolution in the case of the African or Asiatic languages, where the orthodox subject-predicate system does not exist. Here, then, is an important subject for the future.

The fourth acquisition to the techniques of aphasia research is an unexpected one—namely, *Pavlovian ideology.* On the face of it, this might appear unpromising, being based upon an utterly materialistic philosophy moored to animal observation. But the enlightened interpretation of such workers as Luria,

Beyn, and others demonstrates that Pavlovian research into the evolution and dissolution of language is possible, and may indeed prove valuable.

Questions in Aphasiology

Equipped with these new weapons of research we can now venture upon a study of many problems in aphasiology which have hitherto been obscure. Some of these questions are even now matters of debate: others have not yet been broached. The future years will surely yield answers to such queries as the following.

1. How Far is Aphasia a Localizable Symptom?

Already there has taken place a shift away from a preoccupation with aphasia as a static outfall-symptom of brain disease, localizable to this or that region within the left hemisphere. Localization is not thrown overboard, however, but it has become demoted in rank of significance. The functional disturbance within the province of symbolic thinking is realized to be more complex and usually more intense than can be ascribed to the negative effect of a circumscribed lesion. Many factors are operative, some of them subtle and intangible. The role of diaschisis, and of demential epiphenomena, deriving from the "momentum" of the causative lesion, must be reckoned with and evaluated.

Even though his name is associated with the events due to a discharging lesion of the motor cortex, Jackson was of course the first among neurologists to adopt a dynamic attitude towards the effects of brain damage. As he himself said, "I am neither a universalizer nor a localizer." Since speech and words enter into thought he deemed it incredible that "speech" could "reside" in any limited spot. So far as aphasia was concerned he rarely tried to track down lesions from the clues offered by the disordered speech. He did not believe in abrupt geographical localizations. Very sudden and very extensive damage to *any part* of the left cerebral hemisphere would produce *some* amount of defect of speech.

In our own time Leischner has stressed, like many others, that speech performance is to be looked upon as an overlaid or parasitic function which utilizes preformed brain mechanisms as well as preformed peripheral instruments. No one can seriously claim that the brains of illiterates who have neglected to learn the arts of reading and writing are in any way deficient in "centres" when compared with the brains of the highly educated. Speech is a secondary and not a primary cerebral function, and therefore has no central executive or receptive apparatus of its own. Rather does it utilize, as it develops, brain mechanisms which are already in existence. Individual dispositions may even determine a shift in the centre of gravity of these secondary cerebral functions. This idea is reminiscent of Weizsäcker's "functional migration." In cases of special sense-deprivation the faculty of speech may be looked upon as metamorphosed or transposed, as in the case of the Braille reading in the blind, the sign languages of deaf-mutes, and, most impressive of all, the tactile system of communication in a Helen Keller or a Laura Bridgman, bereft of hearing, sight, and articulation. In such cases the drive towards expression and communication utilizes whatever means happen to be available.

Riese has said that there never will be a cerebral localization of productive thought, since what is really productive and creative in the human mind resists even the most generous and universal localization. Since it is a coming-into-being of what did not exist before, it cannot be correlated with existing material. Riese traced an analogy with the heel of Achilles. Although the heel was the most vulnerable region of the hero's body, and although its injury would be fatal to his life, life cannot be said to be localized at the heel; it pervades the whole body.

2. What is the Ideal System of Classification?

Jackson himself rarely tried to group his cases of disordered expression, but contented himself with descriptive labels such as "recurrent utterance," and "occasional utterance." A splitting into "motor" and "sensory" types came later, the work of others. For many years this apparent logicality served a purpose but with ever-increasing inadequacy. Already neurologists are profoundly critical of the classical Lichtheim–Wernicke classification. Head's classification was a very worthy one, based upon observed psychological data, but it was doomed to fail. Ramon Jacobson, one of the few linguists to concern himself with questions of pathology, has attempted an unusual type of distinction which applies both to normal speech and to patterns of aphasia. This is based upon a contrast between metaphor and metonymy, as representing two basic methods of relation: the one is an internal relation of similarity and contrast, the other being an external relation of contiguity or remoteness. An aphasiac shows impairment in either one, but only one, of these modes of verbal behaviour, and for this reason Jacobson visualizes a "contiguity disorder of speech" as opposed to a "similarity disorder of speech."

Classifications of aphasia based upon levels or functions of normal speech are unpromising, for, as Head pointed out, the types of aphasia we meet with clinically are not fragments of normal speech, and they do not directly reveal the elements out of which language is built.

We may perhaps predict that in the future there will emerge another kind of classification, clinico-psychological in nature. Attention may become directed more and more to the "preverbitum"—that is to say, the silent processes of thinking which immediately precede the act of expression in speech or writing. This rapid but all-important fragment of mentation obviously varies widely in the normal subject according to many ever-changing circumstances, as, for instance, the semantic properties of the emerging words. In aphasiacs the errors of difficulties in word-finding may be the product of blockage which may occur at different levels within this preverbitum. Herein we can detect the possibility of erecting a classification based upon some such notion of levels of thought. Thus the patient who is merely at a loss to supply a word at a given moment to an article presented to him might be deemed to have a word-block at a quite superficial level. The patient with a fluent but wellnigh incomprehensible flow of jibberish has a much deeper defect, and if such an aphasiac is also found not to comprehend the statements of others the defect must be even more profound. Work along lines such as these will surely continue.

3. Does Aphasia Necessarily Entail a Disorder of Intellect, whether Quantitative or Qualitative?

Most would expect the eventual answer to be in the affirmative. Goldstein's important dichotomy between

conceptual and concrete attitudes at one time seemed to supply the solution, explaining both mild and severe cases. Latterly, however, the validity of Goldstein's hypothesis has been questioned, as by Isserlin, Beyn, Luria, Bauer and Becka, Kok, and others. Time will show how far these criticisms are justified. It is difficult to deny that eventually there will surely emerge proof of some affection of intellect, or of personality, or both, running like a scarlet thread through the pattern of all the aphasias. As Marcus Victoria said, "aphasic patients do not see or hear the other world like the rest of mankind. Their defects are deeper than the language defects, and comprise functions correlated with the manipulation of symbols." It is with these various non-verbal defects that future aphasiologists will be deeply concerned.

4. Does the Dissolution of Speech in Disease Recapitulate the Stages of Development of Speech in the Child?

A. F. Watts has proclaimed that ". . . speech development in the child and in the race follows broadly the same lines, and the powers lost as a result of mental derangement disappear in the reverse order of their acquirement, just as in a stricken tree death appears in the newest twigs before it reaches the older branches." I take leave to doubt the validity of this idea, and I believe that aphasiologists of to-morrow will examine with greater care, and more critically, this seductive notion. Here is a facile conception which has appeared in many writings in the past and even at the present time. Some, like Jacobson, have aligned certain types of aphasia with the manner of speaking of a child. Others—like my friend Alajouanine, and also Diamond—have sought to correlate the dysarthric defects in aphasic patients with an infantile fashion of talk. Both are believed to show a similar pattern of phonemic substitutions, the aphasiac stumbling most over consonantal sounds which a child masters comparatively late. This is what has been called the "syndrome of phonetic disintegration." I have never been impressed by this relationship and I am still dubious. Professor Fry, of the London University Department of Phonetics, has subjected one of my aphasic patients, chosen at random, to a most rigorous speech-analysis. His research completely failed to reveal any hint of a reversion to a less mature manner of articulation.

Time will show whether it is logical or appropriate to seek an analogy between the defect of speech from disease in an adult—that is to say, one who had attained linguistic maturity and then lost it—and the ontogeny of speech. At the present time it is safer to assume an attitude of scepticism and to avoid drawing parallels too freely. If we really wish to find a disease state which recapitulates the infancy of speech we are more likely to witness it either in the dilapidated utterances of a dement or, better still, in the baby-talk of a hysteric.

5. What is the Essential Nature of the So-called Congenital Dysphasias, Including Developmental Dyslexia and Congenital Auditory Imperception?

So far we are merely at the stage of observation and recording. But already the available evidence clearly shows that these are not "pure" or delimited defects as was originally imagined. To what extent they depend upon subtle inborn disorders of simple perception is a problem for the future to unravel. Whether in fact there exists any underlying structural defect is uncertain, and would appear to-day to be unlikely. Whether the dyslexia or dysphasia is merely one aspect of a deeper defect of a spatial or of some other symbolic quality is a matter for future neurologists.

6. How Far is it Correct to Align So-called "Motor" Aphasia with Apraxia, and "Sensory" Aphasia with Agnosia?

Since Liepmann's work in 1900 opinion on this subject has oscillated. To-day we are sceptical of isomorphism of this sort. The conception of any such pure entity as "motor" aphasia is out of favour. Correlation of a cerebral dysarthria—that is, a disorder due to a focal cortico-subcortical lesion, with an articulatory apraxia—is, however, still conceded. Further than that modern neurologists are unwilling to go. We may re-echo the words of Bay, who, concerning apraxia and aphasia, said, "The two have as little in common as the leaping attack of a bird of prey with the strategic planning of the general staff."

7. To what Extent are the Receptive Defects in Aphasia Dependent upon an Impairment in the Perception or Utilization of Simple Sense-data?

It may well be found that the reception of auditory or visual signals is imperfect, or perhaps abnormally delayed, in aphasiacs. Tachistoscopic testing is likely to demonstrate such a state of affairs. Or, on the other hand, the defect may lie at a deeper level—namely, within the patient's frame of expectation—for in normal circumstances an anticipatory state materially assists the correct reception of signals. Sensory aphasia may turn out to entail an impairment of this "prior set." These are straightforward questions which will assuredly be answered in the future.

8. How Far Does the Problem of an Aphasia Depend Upon Individual Pre-morbid Habits of Speech?

Considerably more attention is due to the subject of the aphasic patient's previous educational status, with special reference to his literary attainments, habits, prejudices, and predilections. The performance of an aphasic patient is now looked upon as a variable, based upon a formula entailing not only such obvious factors as the size and locus of the lesion, its nature, its chronogenic properties, and its degree of abruptness, but also the make-up of the victim with particular respect to his pre-morbid literacy. The aphasiac's performance will also depend upon a complexus of immediate circumstances, both extrinsic and intrinsic. As Goldstein has put it, the brain-injured person is struggling to cope with a more or less artificial test-situation by utilizing as best he can the attenuated and reduced mechanisms available to him at that particular moment. And in so far as each one of us possesses his own idiolect, the use of language is ordinarily a very personal mode of behaviour. Aphasia must therefore constitute an aberration in the pattern of total behaviour rather than a scotoma within the field of language-function.

Factors of age are of course of obvious importance. It is still uncertain, however, whether the sex of the patient in itself exercises any influence upon the final picture of an aphasia.

This fascinating idea also ties up with the problem of the earliest appearances of speech in *Homo sapiens*. While some evidence can be adduced to suggest that among our prehistoric forebears speech was a masculine prerogative, equally specious arguments are available to the effect that speech acquisition was mainly due to the enterprise of the female sex.

These considerations were envisaged long ago by Jackson when he spoke of the influence of the "four factors of the insanities." The factors as he originally set them out in 1874 were: (1) the depth of the dissolution or reduction; (2) the rapidity of the reduction; (3) the kind of brain in which the reduction occurs; and (4) the influence of external circumstances and internal bodily states on the patient who is reduced. It is Jackson's third factor which augurs so well for future investigations.

Conclusion

According to Lenin, "one fool can ask more questions in a minute than twelve wise men can answer in an hour." None the less, I believe I am justified in trying to trace some of the steps which aphasiologists will take in the future. The problems I have outlined are all of such a nature as would surely have intrigued Hughlings Jackson were he still with us. These questions of to-day and to-morrow reflect the enduring influence of Jacksonian principles, and the stimulus of his ideas continues to guide our investigations and our thinking. So far as the subject of language and its disorders is concerned, the future of neurological research is most certainly assured for yet another century.

BRAIN, MOVEMENT AND TIME*

BY

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It is one hundred and three years since the auspicious day that Victor Alexander Horsley was born; and forty-four years have passed since he bowed to human frailty in the sixtieth year of his life in the midst of his last inspired and inspiring campaign for his country and for his profession. One hundred years have passed since the founding of the National Hospital that he served so loyaliy and with such distinction. We meet here in this hall, and under the chairmanship of the President of that professional association in which Sir Victor played so vital a part. We are met here to pay homage to a great man, a distinguished neurologist and a leader in surgery —Sir Victor Horsley.

I am persuaded that Sir Victor is not dead. The knowledge and the impetus that he gave to medical science and technique live on—increasing in significance as following generations build and will continue to build upon them. We may feel the joy that we believe he feels in the centenary celebrations of his hospital, the pride that he has in the magnetic influence of Queen Square, which he helped to increase in his mortal days, and which continues to increase in force and scope to this present. If I read his thoughts aright he views with favour and admiration the achievements of the British Medical Association in these days; and its Royal Presidency must give him the deepest satisfaction.

Sir Victor was a surgical neurologist. I am indebted to his successor at University College—the late Sir Wilfred Trotter—for the phrase. Sir Victor was a devoted clinician. It has been well said that Queen Square was and is the cradle of neurology. Sir Victor brought the humane grace of surgical therapy to attend the infant in that cradle—the clinical science of neurology. He pioneered surgical neurology as a specialized clinical discipline. He was an experimental physiologist. The clear and purposeful planning of his investigations yielded to him important scientific knowledge in spite of the relatively crude techniques then available.

The living pathology and especially the mechanical pathology of the nervous system also received Sir Victor's attention and interest, as witness his work on the mechanism of papilloedema and on the effects of experimental cerebral compression. It is in this latter field—that of the living and moving pathology of cerebral displacements—that I propose to present some comments that I believe would interest Sir Victor and may, I hope, satisfy the Memorial Trustees.

The title I have chosen—"Brain, movement and time"—is intended to imply simply the effect on the brain of its abnormal movement in relation to its containing coverings; and the differing effects of the varying periods of time in which these movements may take place. In other words, I shall endeavour to survey the vital pathology of the brain under stress of displacement at various time rates, the clinical effects and the principles of their management.

Anatomy, Physiology, and Pathology

The containing coverings of the brain, the skull, the dura mater and its partitions, constitute two forebrain compartments and a hind-brain compartment connected with each other by the "narrows" at the archway under the falx cerebri and at the incisura tentorii. When the brain is displaced the linear displacement is greatest at these "narrows." The anatomical arrangement of the blood supply is such that the arterial circle of Willis is relatively fixed to the skeleton of the head. The perforating arteries of the base cross the subarachnoid spaces in their short course from the fixed arterial circle to the overlying brain; and here they are peculiarly vulnerable. Under certain pathological conditions the brain may move extensively in relation to the fixed circle. The delicate perforating arteries are stretched, attenuated, and their calibre is reduced or occluded. There ensues ischaemia, hypoxia, or infarction in their territory of supply. This includes the diencephalon and mid-brain, containing the reticular formation, the archipallium, and the hypothalamus. Ischaemia in this field finds clinical expression in impairment of consciousness, alterations of emotional state, and derangements of homoeostasis in several fields —notably control of body temperature, of respiration, of visceral motor and secretory function, and of pituitary endocrine function. The long tracts traversing this zone may suffer hypoxia.

The time factor is important in relation to brain displacements. If the displacement is slow enough the dural partitions yield considerably and so mitigate the effect; and the arteries adapt themselves to the deformation without loss of calibre until displacement becomes extreme. On the other hand, the more rapid the displacement the severer the effects as regards herniation through rigid apertures at the "narrows" and as regards early arterial occlusion. Abrupt displacement adds another factor. Sudden stretching of an artery causes spasm of its walls, and the occlusion and ischaemia due

*The Victor Horsley Memorial Lecture (slightly abridged), given at B.M.A. House, London, on June 24, 1960.

to such spasm may last for seconds, hours, or days, according to the severity of the traumatic stimulus.

Brain Displacement Syndromes

The principal clinical groupings associated with what I may designate brain displacement syndromes may be conveniently considered in four categories arranged according to the rate of displacement. (1) Those due to slowly expanding, displacing intracranial lesions, for example, slowly growing neoplasms, chronic abscesses, chronic subdural haematomas. The duration of displacement is over a period of years to a few weeks. (2) Those caused by rapidly expanding, displacing lesions—for example, rapidly enlarging neoplasms, acute abscesses, acute intracranial haematomas. The duration of displacement is from a few weeks to a few days. (3) Those due to the abrupt and temporary displacement occasioned by basal subarachnoid haemorrhage from rupture of a cerebral aneurysm. The duration of displacement is a few minutes to a few seconds, but the effect may be prolonged for minutes or days by arterial spasm. (4) Those due to the sudden, temporary brain displacement occasioned by dynamic head injuries. The duration of displacement is a fraction of a second. The duration of consequent arterial spasm may be seconds or days.

The clinician recognizes a very similar clinical picture in each of these four categories: in the patient with brain tumour in whom coma has supervened; in the patient afflicted by the apoplexy of acute spontaneous subarachnoid haemorrhage; and in the unconscious victim of dynamic head injury. There is the same unconsciousness, overbreathing, raised temperature, intestinal stasis, oversecretion in pharynx, bronchi, and stomach, bilateral extensor plantar response, and sometimes a "decerebrate" type of rigidity. This is the syndrome of severe diencephalic ischaemia. No less striking is the similarity of the effects of lesser grades of diencephalic ischaemia in the four categories. The milder clinical syndrome is evidenced mainly in impairments of consciousness—defects of memory retention, restrictions of perception, and inability to sustain attention. It is seen in the progressive expanding lesions—as a late symptom in the slow forms and as an early symptom in the more rapid; it appears during their process of dissolution of function. It is seen during the process of resolution of function in patients recovering from the coma of apoplexy or of head injury; and, in them, as the last evidence of a resolving diencephalic ischaemia.

The Common Pathological Basis—Diencephalic Ischaemia

The pathologist recognizes a similar ischaemic pathology in each of these displacement syndromes. I think we have been tardy in recognizing the ischaemic nature of the pathology because ischaemia sufficient to abolish function may produce no changes recognizable by naked-eye inspection after death; and not even to microscopic scrutiny until it has lasted for at least 24 hours before death. Indeed, it is only when the ischaemia is so severe as to cause haemorrhagic infarction, with those characteristic mid-brain and diencephalic haemorrhages, that it is easily seen. Significantly, they are similar in pattern in cases of death from tumour displacement, from acute basal subarachnoid haemorrhage, and from severe dynamic head injury.

While each of the clinical conditions mentioned has the evidence of diencephalic ischaemia as the common feature and as its central feature, each has its own particular pattern of symptomatology grouped round the central feature in time and space. We may survey each briefly.

The Slowly Expanding Intracranial Lesions

In these conditions, progressing slowly over years or months, symptoms and signs originating at the locus of disease may be strikingly evident—for example, by local epilepsy, hemiparesis, dysphasia, or hemianopia—or they may be absent. Next come the train of symptoms and signs dependent on secondary hydrocephalus, including papilloedema and other patterns of neurological disorder that we have learned to associate with cerebrospinal-fluid obstruction and accumulation. The secondary hydrocephalus is usually the precipitating factor of the next, third, phase—signs and symptoms caused by cerebral displacement. Thus, late in evolution of the slowly expanding lesions cerebral displacement reaches a point at which dural yielding and vascular adaptation can no longer compensate it; and the arterial blood supply to the diencephalon and mid-brain begins to suffer.

Headache signalizes stretching of the perforating arteries. Consciousness begins to show impairment in defect of memory retention, restriction of perception, and failure to sustain attention. As these symptoms deepen to coma, respiration increases in rate and depth, the body temperature rises, there is excess of secretion in the pharynx, bronchi, and stomach, there is gastro-intestinal stasis, and the plantar response becomes bilaterally extensor. As the brain-stem is thrust down, an abducent nerve palsy appears. A variable but common feature in these cases is evidence of hypopituitarism.

In these slowly expanding lesions I think we understand the mode of production and the expected patterns of symptoms, their significance, and the possibilities of misinterpretation. We have recourse to one or more ancillary modes of investigation when in doubt about the site and nature of the lesion and the direction of its management. With this knowledge of the problem and with these aids it is now rare for the victim of a slowly expanding lesion to reach the stage of coma.

Treatment aims, firstly, at relieving dangerous cerebral displacement and, secondly, at eradication of the underlying disease. In the rare cases in which severe impairment of consciousness has supervened, treatment aimed at combating the diencephalic ischaemia must be added—as is discussed below in relation to head injuries.

It is worth reflecting that when the patient with a slowly expanding intracranial lesion begins to complain of headache he is really complaining of stretching of his basal perforating arteries. When he mentions vomiting he signalizes hypothalamic ischaemia. Forgetfulness means archipallial ischaemia. Papilloedema portrays hydrocephalic distension of his optic-nerve sheath. Thus interpreted these symptoms of brain displacement are alarming and urgent, and properly so—for at any moment irreversible infarction in diencephalon or mid-brain may supervene.

Rapidly Expanding Intracranial Lesions

The rate of displacement is more rapid, extending over a few weeks or a few days. The perforating

arteries have less time in which to adapt to deformation; and the dural partitions remain relatively rigid.

Early headache signalizes tension in the arteries; and at an early stage vomiting and impairment of consciousness indicate diencephalic ischaemia. Any symptoms originating at the primary locus of disease tend to be lost in the deepening coma. Hyperpnoea, hyperpyrexia, and hypersecretion soon appear, and the bilateral Babinski sign and decerebrate rigidity may follow. Through the still rigid tentorial aperture the temporal lobe hernia is thrust, carrying the oculomotor nerve before it and thus causing the homolateral dilated pupil and external ophthalmoplegia. This is in contrast to the abducent-nerve palsy of the chronic case. Also in contrast is the greater frequency of homolateral spastic paresis in the rapidly expanding lesions—due to the thrust of the opposite crus against the rigid tentorial margin as the hernia displaces the brain-stem to the opposite side.

Again I think we have become familiar with the cerebral displacement syndromes in these more rapidly displacing lesions—with the proper interpretation of their clinical signs and with their possible misinterpretation.

The demand for treatment is still more urgent, for at any moment the diencephalic ischaemia may advance to irreversible ischaemic haemorrhagic infarction. The primary object in treatment is the timeous correction of the cerebral displacement, and so the restoration of an adequate blood supply to the diencephalon and midbrain. The clot is removed, or the abscess is tapped, or local contusional swelling of brain tissue is afforded generous decompression. This is often not enough; for with a rigid tentorium and an impacted hernia the displacement requires more positive restitution. This is achieved by the rapid injection of normal saline solution into the theca while the head is still surgically open. By this manœuvre the hernia is pushed back through the tentorial aperture. Often the patient wakens dramatically from coma as this is done. One can visualize the pleasant pink blush from restored arterial supply that pervades his mid-brain as this occurs. We call the procedure "positive disimpaction."

When, in severe cases, the effects of basal ischaemia persist, those measures are pursued to promote an effective circulation and to minimize the effects of ischaemia, as detailed later in connexion with head injuries.

Abrupt and Temporary Expanding and Displacing Lesion of Basal Subarachnoid Haemorrhage from Aneurysmal Rupture

The rate of displacement is still more rapid—a few minutes or a few seconds. As the basal cisterns rapidly fill with fluid arterial blood, the brain is displaced from the base of the skull and from the fixed arterial circle of Willis. The slender perforating arteries are rapidly stretched and attenuated and their territory is rendered ischaemic. The patient may cry out complaining of severe headache as his arteries are stretched; and he collapses in apoplectic coma as diencephalic ischaemia supervenes. The blood, which remains fluid in the subarachnoid spaces, soon disperses and the displacement subsides. The sudden stretching of the arteries has, however, induced spasm of their walls, so that the duration of ischaemia is prolonged; while it lasts, perhaps for minutes, perhaps as long as 12 days, the patient remains comatose. As the arterial spasm relaxes and the diencephalic circulation recovers coma lightens to a state of impaired consciousness or confusion. Recovery may be rapid and complete. In the severer cases when coma is prolonged it is usually accompanied by clinical evidence of hypothalamic ischaemia and dysfunction—hyperpnoea, hypersecretion, gastric haemorrhage, gastro-intestinal stasis, hyperpyrexia; often a bilateral Babinski response develops. The blood-pressure usually rises initially—a reflex attempt to compensate hypothalamic ischaemia. Later it may fall and prove difficult of maintenance—an evidence of pituitary and suprarenal insufficiency.

Exact localizing evidence of the underlying aneurysm is usually absent, as the haemorrhage occurs into a free space. Symptoms and signs peculiar to acute basal intracranial haemorrhage include subhyaloid or vitreous haemorrhages from acute distension of the optic-nerve sheath by the extravasation; and when consciousness has been regained the features of meningeal and sensory nerve root irritation are evident. Blood is found in the cerebrospinal fluid on lumbar puncture.

Not infrequently some part of the extravasation penetrates into the brain substance. In this environment the extravasated blood clots. It then constitutes a rapidly expanding, displacing, intracranial lesion, which requires appreciation from its clinical syndrome and from angiography.

Management of these cases is largely controlled by the progress of restitution of consciousness—that is, of evidence of recovery of the diencephalic blood supply. Until this is restored angiography is dangerous as it may aggravate the ischaemia. In the mildest cases, when confusion clears within a few hours, angiography can then be proceeded with, and treatment of the aneurysm to prevent further bleeding can follow it at once. In the severer cases treatment to mitigate the effects of diencephalic ischaemia and to promote diencephalic blood supply must be instituted and maintained until consciousness is regained and confusion has largely recovered. Angiography and treatment of the aneurysm must await this recovery in spite of the risk of further haemorrhage during the waiting period, which may vary from a few hours to several weeks.

Intracerebral or subdural haematomas require treatment, in their own right, as rapid expanding, displacing intracranial lesions. It is worth noting that infarction of any large cerebral territory, which may arise in connexion with the treatment of a cerebral aneurysm, is associated with severe swelling of the affected brain tissue and may require adequate surgical decompression.

During local operations for cerebral aneurysms we may find the artery in a state of spasm or the surgical manipulations of the artery may induce severe spasm of it. Papaverine solution applied direct to the exposed arterial wall causes visible relaxation of this spasm in about five minutes. Indeed, we have sometimes left a small plastic tube in place so that we can inject papaverine solution to bathe the arterial wall at suitable intervals after such operations and so guard against recurrence of spasm. I do not know of any substance that can be administered systemically that has a similar effect on this traumatic type of local arterial spasm. If such a substance were available, I believe many of our problems of the diencephalic ischaemia associated with cerebral displacement could be resolved.

Abrupt Temporary Displacements of Dynamic Head Injuries

Concussion

By the qualification "dynamic" we indicate those head injuries associated with abrupt acceleration or deceleration of the head in space, with their transient deformation of the skull at the site of impact and their associated forces of momentum and of inertia. These factors cause the brain to move extensively within the skull. The displacements occupy but a fraction of a second. Consequent arterial spasm may last for seconds or for days. These head injuries are of increasingly frequent occurrence, and constitute an important social problem and a surgical challenge.

The transient deformation of the skull drives the brain to the opposite side under the falx and also down through the tentorial aperture. The anterior and posterior groups of perforating arteries are abruptly stretched. The elastic skull rebounds to its original form—in the absence of comminuted fracture—and the arteries are jerked back. The force of momentum now takes over and displaces the brain towards the site of impact, and the arteries are tugged in this direction quite extensively. There results almost immediate diencephalic ischaemia and loss of consciousness. As this abrupt tugging of these arteries induces spasm of them the effect on the diencephalon is less or more prolonged. In the mildest cases there may be only impairment of consciousness for a few seconds. In the severer cases spasm can probably continue for a week and unconsciousness for much longer. I suggest, then, that diencephalic ischaemia, so occasioned, is the pathological basis of clinical concussion. It may recover rapidly and completely. It may leave residual infarcts of greater or lesser extent. In the severest cases it is rapidly fatal, and may show the characteristic haemorrhagic infarction of severe ischaemia in the perforating artery and mid-brain territory, quite similar to that seen in expanding lesions. I believe, then, that in treating a patient with concussion we are, or we should be, treating him for diencephalic ischaemia.

In the severer cases the accompanying hypothalamic disorders, expressed as hyperpnoea, hypersecretion, vomiting, gastro-intestinal stasis, gastric haemorrhage, hyperpyrexia, bilateral Babinski sign, and decerebrate rigidity, soon follow the initial loss of consciousness.

The management of this state resolves itself into measures designed to promote an adequate diencephalic blood supply on the one hand, and to mitigate the effect of diencephalic ischaemia on the other.

Thus oligaemia, if it exists from external or internal blood loss, must be corrected; and effective fluid intake to maintain the blood volume must be ensured. The quality of the blood supply in respect of oxygen content requires a clear airway from nose or mouth to lung alveoli; and a sufficiency of appropriate nutrition must be maintained.

Mitigation of the effects of diencephalic ischaemia requires artificial regulation of the body temperature. In most cases the effect of the hypothalamic disorder is to interfere with the reflex mechanisms for thermostasis by loss of heat, and hyperpyrexia results. This increases tissue demand for oxygen which is already in short supply to the ischaemic diencephalon. A vicious circle is established and the temperature soars. The temperature must be reduced by artificial cooling; and heat production must be minimized.

In practice the application of these principles requires transfusion of blood if necessary and the administration of sufficient fluid and nutrition daily, intravenously at first, and by gastric tube as soon as the gastro-intestinal tract is available. The gastric tube is inserted early to control gastric accumulation and prevent dangerous regurgitation. There must be no impediment to pulmonary ventilation, for the slightest fall in blood oxygen aggravates the local diencephalic hypoxia. This is secured as may be required by posture—snoring in these circumstances can be fatal—by temporary tracheal intubation, or by tracheostomy. Unfortunately many patients with head injury vomit and aspirate gastric contents into the airways before they come under medical care. This may require early bronchoscopic clearance; and later this measure may have to be repeated to clear bronchial hypersecretion. If the available lung tissue has been reduced by atelectasis oxygen administration and antibiotics to prevent infection are required.

The temperature should be maintained at normal or a little below it. Cooling is achieved, as required, by exposure of the body surface at an open window, by the application of a moist sheet corresponding to artificial sweat, or the use of actual surface refrigeration. Heat production is minimized by chlorpromazine to control shivering and physical restlessness, and pethidine to control overbreathing. In extreme cases, and especially when there is extensive muscular spasm or rigidity, the use of the potent relaxants and of the artificial respirator are necessary.

Hypersecretion and gastric haemorrhage are dealt with by administration of atropine. Failure to maintain blood-pressure in spite of adequate fluids may indicate acute pituitary deficiency and require a maintenance dosage of A.C.T.H. Direct steroid therapy is to be avoided on account of the liability of these patients to gastric haemorrhage and to pulmonary infection. Occasionally gastric stasis may require the prolonged use of gastric aspiration and of intravenous administration of fluid, electrolytes, and nutrition. The care of the skin, lungs, and kidneys of these unconscious patients requires frequent change of their posture. Mouth hygiene is important; the eyes may require protection from undue corneal exposure; and the convenient disposal of urine and faeces requires attention.

It is important to bear in mind the aggravating effect that pre-existing cardiac, pulmonary, or renal disease may have upon diencephalic ischaemia; and to institute appropriate treatment concomitantly with that for the brain condition. Similarly, uncontrolled diabetes, hepatic insufficiency, or ill-advised "sedative" drugs may aggravate the effect of cerebral ischaemia by their interference with cell metabolism; and suitable countermeasures are required.

It may be noted that the hyperpnoea associated with the local diencephalic hypoxia of dynamic head injuries is what one might term an erroneous reflex. The body has only one response to oxygen lack—to breathe more; and this is a valid response to natural circumstances of increased oxygen consumption and to the pathological circumstance of impediment of the airway. As the diencephalon contains the neural mechanisms for this reflex, local hypoxia of the diencephalon from local cerebral ischaemia sets reflex hyperpnoea in action quite erroneously and uselessly. As the muscular effort of hyperpnoea gives rise to heat production it is actually harmful and should be artificially suppressed.

Similarly, the shivering reflex, spontaneous or provoked by surface cooling of the patient in hyperthermia, is a deranged reflex due, in this instance, to derangement of the diencephalic thermostatic mechanism. The threshold for its activation becomes set too high. Thus the patient begins to shiver with a body temperature of 103° F. (39.4° C.) or more. Again the doctor must step in to abolish this harmful heat-producing reflex activity and permit reduction of body temperature to a normal level.

Secondary Expanding Lesions

In addition to the diencephalic ischaemia of concussion, the abrupt brain displacements of dynamic head injuries may inflict damage that initiates the later development of a rapidly expanding, displacing, intracranial lesion. These secondary lesions may show their presence in a few hours, days, or weeks after the injury. Such are the extradural haematomas, initiated by the rebound of the indented skull from the underlying dura or by fracture of the skull and rupture of the middle meningeal artery; the subdural haematomas from the venous ruptures of "contre-coup"; or the lacerations and venous ruptures as the moving brain encounters the sharp sphenoidal ridges or tears a vein crossing the subdural plane; the local cerebral contusion and oedematous swelling occasioned by similar injuries or by the spread of traumatic phlebo-thrombosis. If such a complication arises in a patient who has suffered relatively brief concussion and has already regained consciousness, we have the classical syndrome of the "lucid interval" before the secondary lesion again causes clouding of consciousness by its secondary displacement effects. If unchecked it rapidly produces severe diencephalic ischaemic effects, and at any moment may cause irreversible haemorrhagic infarction. In these cases the correct assessment is clear and the indications for relief are urgent.

On the other hand, I know of no clinical problem more difficult than the diagnosis of a secondary, expanding, displacing process in a patient who is still unconscious from the initial concussion. The secondary process by its displacement intensifies the signs already present from concussion. To ascertain an intensification of signs in a comatose patient with a severe diencephalic ischaemic syndrome is no easy matter, for it is a repetition of the same cerebral insult before the effect of the first has passed off. It should be noted that the cerebral tissue is much less tolerant of a second insult than of the first, and this accentuates the need for early recognition and treatment. In circumstances of doubt it is obligatory to ascertain the absence or presence of such a secondary expanding, displacing lesion at once, usually by direct surgical inspection through multiple exploratory burr-holes. Treatment of secondary expanding lesions in head injuries varies with their nature. It may consist in the removal of clot or wide decompression of an oedematous part of the brain. One should err on the side of generous decompression, for there is often a phase of oedematous swelling of compressed cerebral tissue after clot removal which should be anticipated. In most of these cases "positive disimpaction" is advisable as the final step of the operation before the head is closed.

Fibre Ruptures

In addition to the diencephalic ischaemia of concussion which may recover spontaneously or may do so under appropriate management, dynamic head injuries may cause direct rupture of axons in the cerebral white matter, especially of the corpus callosum and the centrum ovale, as has been shown by Dr. Sabina Stritch at Oxford. Extensive damage of this nature accounts for many of the early fatalities from severe head injuries. Some cases show gross, visible disruptions; but in others the lesions are not obvious and require careful microscopic elucidation by special methods. These lesions may account for the occasional cases in which signs of basal ischaemia soon settle but which remain with more or less spastic paresis, and with varying degrees of apathy or stupor. Curative treatment of these lesions would appear at present beyond our reach.

Variants of the Concussion Syndrome

I have mentioned the clinical syndrome most frequently associated with severe concussion; and I have expressed the view that its cause is diencephalic and mid-brain ischaemia. There are variants from the typical syndrome whose causes we do not understand in terms of the particular parts of the brain affected or spared. Occasionally, with profound coma, there may be an abnormally low body temperature, and respiration may be normal or slow. Sometimes the blood-pressure may remain low in spite of a sufficient blood volume. Sometimes the initial gastro-intestinal stasis, which usually resolves spontaneously after a day or two, may persist for several weeks. These, and other variants, require further classification, analysis, and pathological correlation.

Conclusion

I would make a plea for adoption of the term "brain displacement" in preference to "cerebral compression" as more expressive of the living pathology that exists. I would urge the use of the term "dynamic head injury" in classifying head injuries, to identify those in which the forces of momentum and inertia play a major part in damage to the brain. In some quarters this generation still seeks a physical sign upon which to base decision and action; and insufficient attention is paid to the psychological manifestation of impairment of consciousness as a neurological sign. The endocrine glands and hormones should be regarded as part of the effector mechanism of the nervous system. The neuronal communications may be compared to a telephone communication system—and the endocrine glands to transmitters, and their hormones to emanations, of a broadcast section of the communication system.

Sir Victor Horsley shows us how he, throughout his life, sustained by faith and courage, without aid of large research appropriation, combined an active surgical career with continued laboratory research work. He sustained an exacting surgical hospital practice; but, at great sacrifice, he restricted it to the sphere of action he had chosen. Throughout his life he prosecuted related laboratory work. He teaches us that clinicians, who meet the problems, must personally devote a substantial part of their endeavour to their solution in the laboratory. He would insist that in our hospital staffing arrangements to-day ample provision should be made for part-time clinical work combined with part-time laboratory investigation, both for young men in training and also throughout life for those with aptitude in both fields; and that in the administration of our ample research funds, sufficiently attractive means should be devised to sustain such combined research and clinical activities.

AUTOIMMUNE COMPLEMENT-FIXATION REACTION IN 1,014 PATIENTS

BY

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Gajdusek (1957, 1958), and Mackay and Gajdusek (1958) reported that fixation of complement occurred when sera from certain hospital patients were incubated with simple saline extracts of various human organs. They called this the "autoimmune complement-fixation reaction" (A.I.C.F.). It had no strict organ specificity, and it occurred most often in cases of liver disease, diffuse "collagen" disease, and macroglobulinaemia. Gajdusek (1958) gave his reasons for regarding the reaction as one between antibody and antigen, and for adopting the view that it is an "autoimmune" phenomenon.

We have looked for this A.I.C.F. reaction in the sera of 1,014 medical patients in the Royal Adelaide Hospital, and report the results, together with a discussion of some possible interpretations of the reaction other than on a basis of autoimmunity.

Materials and Methods

Source of Sera

Blood was taken as a routine from patients admitted to the beds of the professorial unit of the Royal Adelaide Hospital. Other sera were obtained from time to time from large groups of patients in other medical clinics of the hospital. A few specimens were taken selectively from cases of syphilis, yaws, cirrhosis, diffuse "collagen" disease, or from cases known to have abnormal serum protein electrophoretic patterns. Usually only one test was made on each patient, and this was soon after admission or in an acute phase of the disease, when diagnosis or management was under active consideration. Every one of the 1,014 cases was later reviewed and a diagnosis assigned without reference to the A.I.C.F. results, which were recorded separately.

Complement-fixation Test

Complement.—Pooled guinea-pig serum was stored in small amounts at −20° C.

Antigens.—Fresh organs, obtained surgically or at necropsy, were homogenized to a 10% suspension in physiological saline in a Waring blender, then centrifuged three times at 3,000 r.p.m. for 10 minutes at +4° C. and the sediments discarded. The supernatant solution was the antigen, and was stored in small containers at −20° C. for up to three months. Antigens were prepared from normal liver, kidney, lung, adrenal, and thyroid gland.

Diluent. — Calcium - magnesium saline was used throughout the test (Mayer *et al.*, 1946).

Technique.—A five-volume technique, using 0.2-ml. volumes in Wassermann tubes, was employed. Sera were inactivated for 30 minutes at 56° C. before testing. Serum dilutions, antigen, and $2\frac{1}{2}$ HD_{50} of complement, titrated previously in the presence of antigen, were allowed to stand overnight at +4° C. and then for one hour at bench temperature. Two volumes of haemolytic serum were then added to each tube and incubated at 37° C. for 30 minutes, after which the cells were sedimented by light centrifuging. 50% haemolysis was taken as the end-point. Each test was accompanied by a serum anticomplementary control, and known positive and negative sera were included in each batch of tests. Sera were initially screened at 1/10 and 1/80, and then titrated fully if complement-fixation occurred. A "positive result" was complement-fixation at 1/10 or a higher dilution. There were 10 sera among the 1,014 which were anticomplementary at 1/10 without antigen, and we regarded these as giving a negative A.I.C.F. reaction.

Results

The results are given in Table I, from which it is clear that many sera fixed complement with several antigens, rather than with one only; in fact, this was the rule and not the exception. Neither a characteristic pattern of activity with a group of antigens nor any reciprocal relationship between antigens could be seen on an ordinary inspection of the results, except that, of the five antigens used, kidney and liver were most regularly among the positive reactors. (Liver, kidney, adrenal, and thyroid antigens were used to test all the 1,014 sera, but only 903 of them were tested with lung. Consequently the appropriate reduced total of cases tested with lung is shown in each disease category in Table I.)

The allocation of patients to groups of diseases in Table I was made after a review of every case and without reference to the serological results. The association of diseases within the groups are apparent in most of them. Group 4 is one of the loosest, comprising the theme of vascular insufficiency in a broad way to include diabetes (with its arteriosclerotic complications) and haemorrhage, as well as cardiac and cerebral infarction, but not periarteritis nodosa, which is in group 7. Viral hepatitis is in group 8. Group 10 shows separately some conditions which may be of interest from the "autoimmune" point of view, but the bulk of this group is made up of undiagnosed cases, with some miscellaneous examples of comparatively rare conditions not classifiable under any of the other heads.

It is clear from an inspection of the table that the incidence of a positive A.I.C.F. reaction in the whole group of 1,014 hospital medical patients is much higher than in 164 apparently healthy blood donors, and that Gajdusek and Mackay's findings in liver diseases, "collagen" diseases, and paraproteinaemia are generally confirmed. Wishing to make useful comparisons between groups of people with different diseases (and not merely between disease and the healthy state), we decided that group 10 represented a suitable control collection of persons who were sick to a similar degree, being admissible to the same wards over the same period in the same hospital under the same physicians, as those in the other groups of more readily defined disease states. Consequently we have made a comparison

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between group 10 and each other group, using the χ^2 test, of the incidence of the A.I.C.F. reaction between the patients' sera and each antigen in turn. Those which vary significantly (for the numbers observed) from group 10 are shown in Table II.

The thyroid gland is the only organ which shows a good correlation between A.I.C.F. activity and clinical disease in the same organ as that from which the antigen derives. We are reporting on this elsewhere (Hackett *et al.*, 1960).

Some virus conditions other than viral hepatitis, particularly infectious mononucleosis, though not necessarily with a positive Paul–Bunnell test, seem to provoke A.I.C.F. activity. The positive reactions obtained in syphilis and yaws are not unexpected when it is considered how similar the A.I.C.F. technique is to the Wassermann reaction.

Group 4 and group 6 show respectively a possible deficiency of anti-kidney and anti-lung activity compared with group 10, but at a low (P=0.05) rate of significance.

An analysis by sex and age was made of 988 of the sera from patients where details of the age could be satisfactorily established. The results showed a higher incidence in females than in males in all decades below 60 years; above this the incidence was equal in the two sexes. The percentages are given in Table III. There was no clear tendency for the incidence of the A.I.C.F. reaction to rise or fall with increasing age in either sex.

We found that not one of the following blood-group antigens was exclusively present or absent in the red cells of all of 10 positive A.I.C.F. reactors taken at random: A_1, A_2, B, O; C, c, D, d, E; Le(a), Le(b);

TABLE II.—*Probability (P) Values for the Statistically Significant Differences Between the Positive Results in Various Groups from Table I compared with Group* 10

Group	Any One of the 5 Antigens	Liver	Kidney	Adrenal	Thyroid	Lung
1	<0·001	<0·001	<0·001	<0·001	<0·001	
3			0·05	<0·01	<0·05	
4			0·05			
6						<0·05
7	<0·01	<0·01	0·02	0·001	<0·001	<0·01
8	0·001	0·02	0·001	0·001		<0·001
9	<0·01		0·05		<0·002	

TABLE I

Group	Disease	Total Tested with Liver, Adrenal, Kidney, Thyroid	Positive with any of these Antigens, or with Lung		Positive with Liver		Positive with Kidney		Positive with Adrenal		Positive with Thyroid		Total Tested with Lung	Positive with Lung	
			No.	%	No.	%	No.	%	No.	%	No.	%		No.	%
1	Syphilis and yaws (W.R.+)	15	13	87	9	60	8	53	12	80	11	73	4	2	50
2	Bacterial infections	68	7		4		5		4		1		65	3	
	Tuberculosis	11	2		2		0		0		1		11	1	
	Total	79	9	11	6	8	5	6	4	5	2	3	76	4	5
3	Viral infections	53	13	25	11	21	13	25	9	17	11	21	53	7	13
4	Diabetes	21	3		3		2		2		2		21	2	
	Peripheral vascular disease, Raynaud's	8	1		0		0		1		0		8	0	
	Atherosclerosis, coronary artery dis., infarcts of heart and brain, cerebral haemorrhage	80	9		5		5		5		5		79	4	
	Peptic ulcer, gastro-intestinal haemorrhage	33	5		3		2		3		4		30	2	
	Total	142	19	13	11	8	10	7	11	8	12	8	138	9	7
5	Carcinoma, sarcoma	176	28	16	14	8	19	11	14	8	10	6	133	12	9
6	Reticuloses	37	9		4		5		4		1		22	0	
	Lymph. leukaemia	10	2		1		2		2		0		10	0	
	Myel.	10	2		1		2		1		0		10	0	
	Myeloproliferative disorders	15	0		0		0		0		0		15	0	
	Para- and dys-proteinaemia	12	4		2		4		2		3		12	2	
	Total	84	17	20	8	10	13	15	9	11	4	5	69	2	3
7	Dissem. L. E.	13	10		8		8		7		9		12	7	
	Idiopathic acquired haemolytic anaemia	6	3		3		2		2		2		5	3	
	Rheumatoid arthritis	31	10		4		7		5		1		24	3	
	Rheumatic fever	18	1		0		1		0		1		18	0	
	Other diffuse "collagen" diseases	15	4		4		3		3		9		13	3	
	Total	83	28	34	19	23	21	25	17	20	22	27	72	16	22
8	Cirrhosis	60	21		14		19		13		8		56	14	
	Acute hepatocellular disease	18	6		3		5		4		4		16	6	
	Total	78	27	35	17	22	24	31	17	22	12	15	72	20	28
9	Thyroid diseases	69	24	30	11	14	16	20	8	10	16	20	73	10	14
10	Glomerulonephritis	15	3		3		3		2		2		13	1	
	Asthma	19	1		1		1		1		1		17	1	
	Hypersensitivity, allergy	5	0		0		0		0		0		5	0	
	Deficiency anaemias	19	3		0		1		1		1		19	0	
	Addison's disease	2	0		0		0		0		0		0	0	
	Nephrotic syndrome	6	1		0		1		1		1		6	0	
	Miscellaneous and undiagnosed	169	31		21		24		9		16		153	18	
	Total	235	39	17	25	11	30	13	14	6	21	9	213	20	9
	Grand total	1,014	217	21	131	13	159	16	115	11	121	12	903	102	11
	Healthy blood donors	164	13	8	8	5	9	6	8	5	3	2	164	6	4

TABLE III.—*Age Incidence of the A.I.C.F. Reaction Shown as the Percentage of Positive Results in 455 Male and 533 Female Patients*

Percentage Positive	Age Groups (Years)					
	0–40		41–60		61–100	
	M	F	M	F	M	F
With any of the five antigens ..	15	22	13	24	21	21
With liver	9	13	9	13	12	13
,, kidney	11	17	9	17	17	16
,, adrenal	11	13	8	10	9	11
,, thyroid	7	14	7	10	8	10
,, lung	6	15	5	14	14	11
Total No. in each group ..	138	149	172	189	145	195

M, N; Fy(a); Jk(a). All 10 were e-positive and Kell-negative, but this would be so with over 90% of the patients in the wards.

We found, as did Gajdusek, that the antigenic activity of the extracts was destroyed by heating to 60° C. for 30 minutes. Unlike him, we found that the activity was not removed by centrifuging at 65,000 *g* for 120 minutes, and so we have concluded that at least some of the antigenic activity in our preparations resides in soluble components smaller than cell microsomes.

Discussion

These findings have confirmed the clinical correlations found by Gajdusek and Mackay. We believe they were right to interpret this "A.I.C.F. reaction" on an "autoimmune" basis. The prevailing climate of opinion suggests that autoimmunity in some auto-aggressive form may be the underlying mechanism in many diseases, particularly some in which this reaction is frequently observed. At the same time there are other possible interpretations which we now consider.

Lipid-lipid Interactions, and Anti-lipid "Biological" Reagins

The lipid levels found in plasma can vary physiologically from one individual to another, between the two sexes, and pathologically in conditions such as hepatocellular disease, nephrosis, diabetes, and atheroma. This applies to characterized lipids such as cholesterol, cephalin, and lecithin, but the same may be true, and for other pathological conditions, of various fats, fatty acids, steroids, bile acids and salts, phospholipids, glycolipids, and lipoproteins.

All cells contain lipids, and the simple "antigen" extracts made for the A.I.C.F. reaction are rich in derivatives from broken cells. If certain tissues have peculiar combinations of lipids these would probably be characteristically represented in the extracts.

The Wassermann reaction (and similar complement-fixation tests for syphilis) is a refined prototype of the A.I.C.F. reaction in the sense that an original simple liver extract has now been replaced by purified cardiolipin. Such reactions are very sensitive to the addition of other lipids, so that a mixture of lipids can show some special activities *in vitro* which its individual components will not. Rapport *et al.* (1959) use the phrase "lipid-lipid interactions" to describe this.

The "biological" false-positive complement-fixations encountered in non-treponemal disease can now be identified by showing that the sera lack antitreponemal activity in the immobilization test. But Kent *et al.* (1958) have shown that such false-positive reactions can be distinguished from true syphilitic ones in ordinary complement-fixation or flocculation tests with cardiolipin antigen, by adding specific amounts of lecithin which at different concentrations lead to a selective reactivity of either the syphilitic or the non-syphilitic anti-lipid. Such an observation makes a valuable practical distinction but does not elucidate the nature of the "biological" anti-lipid reagent. Nevertheless, it suggests how the A.I.C.F. reaction, with its lipid or lipid-rich antigens and probable sensitivity to other lipids in the serum, might depend on a reagent of the same type, and show non-immunological variation in complement-fixation among sera from patients with plasma-lipid abnormalities.

Eastwood (1920), in a review of early experimental work on the nature of the Wassermann reaction, showed how much of this was based on the opinion (which it appeared to support) that the syphilitic reagin was not an antibody arising *de novo*, but a constituent of normal plasma which was physically altered in syphilis and thereby changed from a previously masked state. Mackie and Watson (1926) and Mackie and Finkelstein (1928) showed that the Wassermann reagin was a serum constituent which could be found in heat-sensitive form, being destroyed at 55° C. in many, if not all, normal human sera, but was characteristically heat-stable at 55° C. in the sera of rabbits and certain other animals. In human syphilis it seemed to acquire a heat-stable form so that it survived the "inactivation" or heat treatment (56° C. for 30 minutes) that always preceded the serological tests. Kahn (1950) claimed that a heat-stable "syphilitic" antibody could be found in nearly all human sera if a sufficiently delicate technique was used. If the foregoing is true, the role of this specific globulin reagent (heat-sensitive or otherwise) in the normal body must be considered. If it is present in all people, and is only multiplied or altered physically by disease in some way which does not change its immunological specificity, then it cannot be looked on as an autoaggressive agent; it must have a physiological function, even if the term "autoantibody" is used to describe it.

Kidd and Friedewald (1942) have shown that heat-stable complement-fixing antibodies reacting with simple saline extracts of various organs, particularly liver and kidney, can be found in most rabbit sera, and we have confirmed this. Most rabbits, even though bred in captivity, are not diseased according to current concepts of pathology, so here is an indication that the presence of A.I.C.F.-type antibodies is a normal feature in some vertebrates. If the same were true of man, variations in heat stability combined with lipid sensitivity as outlined above could produce many of the patterns shown by the A.I.C.F. reaction in health and disease without invoking acquired autoimmunity. We are at present planning to investigate the effects of adding lecithin or cholesterol to the A.I.C.F. reaction, and of using complement-free unheated sera.

Enzyme Activity

Extracts used as antigens in the A.I.C.F. reactions must contain cell enzymes. Beeson and Rowley (1959) have shown that kidney has anticomplementary activity, probably because renal glutaminase liberates ammonia which destroys the fourth component of complement. If the sera of certain sick people contained relevant coenzymes or activators, it is conceivable that an apparently specific removal of complement might occur

when serum and "antigen" were mixed. This is another possible non-immunological explanation of the A.I.C.F. reaction. It could be investigated by the use of enzyme inactivators.

Aggregated Globulins

The lists of diseases in which the A.I.C.F. reaction is most commonly positive are similar to those in which "biological" false-positive complement-fixation tests for syphilis are most frequently found (Moore and Mohr, 1952), and are also similar to those where positive results in non-rheumatic conditions are obtained with ultra-sensitive elaborations of the Rose–Waaler test such as the latex-fixation reaction (Dresner and Trombly, 1959). There are indications that such reactions all detect a similar feature in serum which is the presence of abnormal large-molecule plasma globulins, perhaps produced by simple aggregation of smaller normal globulins. The tendency to produce these macroglobulins may be inherited, and be more common in women than in men; it may be accentuated by chronic hepatocellular disease, and may predispose to arthritis and the development of other symptoms associated with diffuse "collagen" disorders. Moore and Lutz (1955) produced evidence showing that in women a "biological" false-positive test for syphilis was often followed within a few years by the development of disseminated lupus erythematosus. This is in accord with the view of Haserick (1955), whose clinical studies led him to conclude that there was a "diathesis" or predisposition to this disease.

Autoaggressive or Not?

If the A.I.C.F. reaction is due to the activity of a macroglobulin or to that of a normal or "natural" reagin (which in the light of this discussion may amount to the same thing), the question remains whether or not it is an antibody–antigen reaction. It may not be, if all true antibodies arise only after classical "non-self" antigenic stimulation. However, if patterned globulins can arise without specific antigenic stimulation in some such way as Burnet (1959) visualizes, through the function of a special or uncontrolled clone of cells, then the reaction can be looked on as the equivalent of one between antibody and antigen in a broad sense, and must be regarded as playing a possible autoaggressive part in the aetiology of the diseases with which it is associated. However, an autoaggressive role for such globulins is not the only possible one, and on present evidence is not substantiated. "Autoantibodies" can sometimes be found in apparently healthy people. There may even be physiological patterned antibody-like globulins which play a normal part in the body's economy, and if this is not kept in mind their activity *in vitro*, in reactions like the A.I.C.F., may wrongly be taken as good evidence for the existence of an aggressive autoimmune process.

Summary

The sera of 1,014 mixed hospital medical patients have been tested for the "autoimmune complement-fixation" (A.I.C.F.) reaction described by Gajdusek (1957, 1958), using simple saline extracts of normal liver, kidney, lung, adrenal, and thyroid gland as antigens.

Some positive reactions were found in most common diseases, but the clinical correlations noted by Mackay and Gajdusek (1958) have been confirmed in that positive reactions, usually with more than one antigen, were found with significantly greater frequency in the sera of cases of liver disease, "collagen" disease, and paraproteinaemia; and also in syphilis and yaws, some viral conditions, and thyroid disease. The thyroid was the only organ which showed some correlation between regular complement-fixation with a particular organ extract and clinical disease in the same organ.

Autoimmune interpretations of the A.I.C.F. reaction are valuable, but others which are discussed above should be kept in mind. These are the possibilities that the effect is a lipid-lipid interaction, or an enzymic artifact, or a phenomenon produced by the practice of heating sera to inactivate them before complement-fixation tests are performed, or that it represents a non-immunological alteration in specific globulins.

We are grateful to Professor Robson and the honorary physicians of the Royal Adelaide Hospital who sent us blood samples and allowed us access to their cases. Dr. Kathleen Maros helped us to check and annotate more than a thousand sets of case notes. Mr. Vincent, of the Red Cross Blood Transfusion Centre in Adelaide, kindly did some special blood-grouping. Miss N. Deering and Miss B. Rainsford gave valuable technical assistance.

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Summing-up a symposium on the prevention and the control of heart disease held last autumn in Atlantic City, N.J., Dr. IRVING S. WRIGHT said: "There are now approximately two million people in the United States who have had strokes as far as we can tell from comparable studies. . . . For the sake of this discussion, we may say that in 80% of the two million a clot has been the critical factor. The remainder have occurred on the basis of haemorrhage, aneurysms, and various other pathological conditions. A million people or more per year suffer from myocardial infarctions. We do not know the exact figure because, as I have said, many are unrecognized. In 73% of the cases autopsied in our study of 1,031 cases of infarction the final closure was due to a clot (a thrombosis). This was the terminal event. We do have weapons to deal with this situation. Studies on anticoagulant drugs have shown in many countries of the world . . . that the usual untreated death rate can be reduced by a third and the complication rate during the first six weeks by approximately four-fifths." (*Amer. J. publ. Hlth*, 1960, **50**. No. 3.)

RUBBER-GLOVE DERMATITIS

BY

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Eczema of the hands is a chronic condition the aetiology of which is often obscure, the prognosis uncertain, and treatment largely palliative. Some cases, however, can be traced to allergic contact sensitivity, and in these the outlook is greatly improved, for a specific cause may be found and removed.

Downing (1933) reported seven cases of dermatitis of the hands, all attributable to one particular brand of rubber gloves, while other examples were described by Traub (1946) and Bettley (1952). Leider *et al.* (1952), investigating 124 cases of sensitivity to rubber articles, found that 17 of them were due to gloves, while Sidi and Hincky (1954) were able to collect as many as 102 cases of rubber-glove dermatitis, most of them being caused by red household gloves. Bonnevie and Marcussen (1944) found that allergy to rubber accounted for 2% of all their cases of sensitivity eczema.

Manufacture of Rubber Gloves

Rubber occurs in the tree (*Hevea brasiliensis*) in the form of latex, which is obtained and collected by cutting the bark. In most cases the latex is converted to solid rubber (crêpe or smoked sheet) on the plantation and exported in solid form, but a certain amount of latex is exported in its original liquid state. A preservative (generally ammonia) is added, and the original rubber content (about 40%) is increased to 60% by a concentration process (Stern, 1954).

Whether made from dry rubber or latex, rubber gloves must be vulcanized to acquire typical rubber-like properties. The vulcanization process consists in combining rubber with sulphur. Chemicals known as accelerators are used to speed up this process. Other chemicals used include antioxidants to increase the life of the rubber articles.

Thick gloves, such as those used by electricians, are made from dry rubber. Domestic, surgeons', and other thin gloves are made by dipping a mould either into a solution in a petroleum solvent of the dry rubber or direct into the concentrated latex which has been suitably compounded with the ingredients above mentioned, and also, if necessary, with pigments.

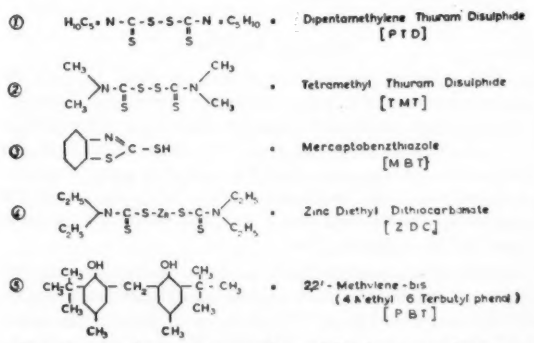
① Dipentamethylene Thiuram Disulphide [P T D]
② Tetramethyl Thiuram Disulphide [T M T]
③ Mercaptobenzthiazole [M B T]
④ Zinc Diethyl Dithiocarbamate [Z D C]
⑤ 2,2'-Methylene-bis (4 Methyl 6 Terbutyl phenol) [P B T]

FIG. 1.—Accelerators commonly used in glove manufacture.

The accelerators used include mercaptobenzthiazole (Fig. 1); thiuram disulphides, such as the dipentamethylene and tetramethyl compounds (P.T.D. and T.M.T.); and dithiocarbamates, such as zinc diethyl, dimethyl, and dibutyl dithiocarbamate.

Antioxidants are not always used with latex, but are generally found in articles made from dry rubber, amine ketone reaction products and substituted phenols being employed for this purpose.

The manufacture of dipped gloves consists essentially in immersing the forma (or mould) into the latex or solution and then drying, vulcanizing, and stripping off the resulting film. The dipping process may be repeated in order to build up a sufficient thickness.

Gloves made from latex are generally leached with water before finally drying and dispatching. This removes soluble products and probably reduces the risk of dermatitis to the wearer.

The compounding of synthetic rubbers follows similar lines.

Investigations

There were 42 patients in the series, 38 females and 4 males. The age at which sensitivity to rubber first developed ranged from 5 to 77 (Fig. 2), with an average of 47.35. Of 30 patients who clearly remembered the

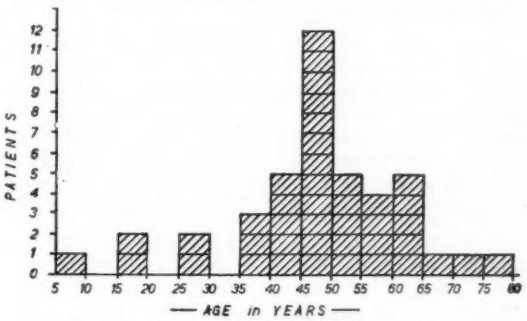

FIG. 2.—Age at onset of sensitivity to rubber.

onset of their rash, 17 had had no skin trouble before wearing gloves, while 13 had started to wear them because they had developed a rash on the hands usually attributed to detergents.

Clinical Features

The backs of the fingers are usually affected, the backs of the hands, and less commonly the palms. The front, back, and sides of the wrists are often involved, particularly at the point where the top of the glove

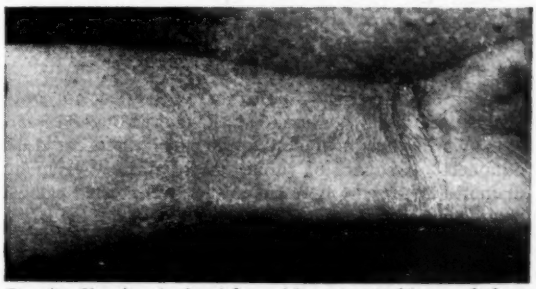

FIG. 3.—Showing the band formed by contact with top of glove.

comes into contact with the skin (Fig. 3). Here a well-demarcated horizontal band of dermatitis is frequently seen (Fig. 4). This may be joined on the ulnar side by a broader, less well defined band extending along the side of the wrist. These should be looked for in every suspected case of rubber-glove dermatitis, as their presence makes the diagnosis practically certain.

In the early case, recognition is more difficult as the rash may be confined to the back of one hand (usually the right) and a small area at the base of the palmar surface of the thumb (Fig. 5).

FIG. 4.—Distribution of rubber-glove dermatitis.

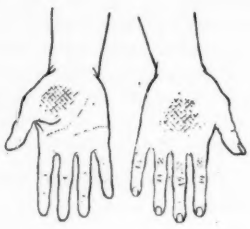

FIG. 5.—Distribution in an early case.

The affected skin is normally reddened and slightly scaling, excoriation marks are common, and vesicles and bullae are comparatively rare.

Other Sites Affected.—Twenty-two patients had suffered from an eczematous rash on other parts of the body. Corsets, or the elastic of brassières or suspenders, accounted for most of these cases (Table I), while several others were attributable to plimsolls or shoes with a rubber insole. Two patients could not tolerate adhesive plaster, and two others developed an acute dermatitis of the face after blowing up balloons. The

TABLE I.—*Other Sites Affected*

Site	Article	Cases
Forehead	Elastic of hairnet	1
Face	Protective face-mask. Balloon	3
Trunk	Corset. Elastic of brassiere	8
Thighs	Elastic of suspender	7
Legs	Rubber-topped socks	1
Feet	Plimsolls. Foam-rubber insoles	7
Various	Adhesive plaster	2

elastic band round a hairnet, elastic-topped socks, and a protective mask used at work were the cause of a rash in three other cases.

Surgical gloves appeared much less likely to sensitize, and 35 tests gave only four positive reactions.

Patch Tests

When the investigation began, patch tests were performed with a single piece cut from a red rubber glove kept for the purpose. In time it became obvious that this was not a reliable test of rubber sensitivity.

After this experience patients were tested not only against samples of household and surgical gloves but also against their own gloves whenever these could be obtained. A square of rubber approximately 1 cm. in diameter was used. In addition they were tested against the accelerators mercaptobenzthiazole (M.B.T.), dipentamethylene thiuram disulphide (P.T.D.), tetramethyl thiuram disulphide (T.M.T), zinc diethyl dithiocarbamate (Z.D.C.), and 2,2′-methylene-bis

TABLE II.—*Results of Patch Tests*

Case No.	Gloves: Household	Gloves: Surgical	M.B.T.	T.M.T.	P.T.D.	P.B.T.	Z.D.C.	A.K.
1	+	−	−	+	+	−	−	−
2	+	−	+	+	−	+	−	−
3	−	−	−	+	+	−	−	−
4	+	−	+	−	+	−	−	−
5	+	−	−	+	+	−	−	−
6	+	+	+	−	−	−	−	−
7	+	−	−	+	+	−	−	−
8	+	−	−	−	+	−	+	−
9	−	−	−	−	+	−	−	−
10	+	−	+	−	−	−	−	−
11	+	−	−	+	+	−	−	−
12	+	−	+	−	−	−	−	−
13	+	−	+	−	−	−	−	−
14	+	−	−	+	+	−	−	−
15	+	−	+	+	+	−	−	−
16	+		+	+	+	−	−	−
17	+	−	−	+	+	−	−	−
18	+	−	+	−	−	−	−	−
19	+	−	−	−	+	−	−	−
20	+	−	−	−	+	−	−	−
21	+	−	−	−	+	−	−	−
22	+	−	+	−	−	−	−	−
23	−	−	−	+	+	−	−	−
24	+		+	−	+	−	−	−
25	−	−	−	−	+		−	−
26	+		−	−	+	−	−	−
27	+		−	+	+	−	−	−
28	+	+	−	+	+	−	−	
29	+	−	−	+	+	−	−	−
30	+	−	+	+	−	−	−	−
31	+	+	+	+	−	−	−	−
32	+		−	−	−	−	−	
33	+	−	−	+	+	−	−	−
34	+	−	−	+	+	−	+	−
35	+		+	−	−	−	−	−
36	−	−	−	−	+	−	−	−
37	+	−	−	−	+	−	−	−
38	+	−	−	+	+	−	−	
39	+	−	+	+	+	−	−	−
40	+	+	−	−	+	−	−	
41	+	−	−	−	+	−	−	
42	+		−	−	−	−	−	−
Total tests	42	35	42	42	42	41	42	37
+	37	4	15	20	30	1	2	0
%	88·1	11·43	35·71	47·62	71·43	2·44	4·76	0

(4-methyl-6-terbutyl phenol) (P.B.T.). Tests were also performed against an amine-ketone reaction powder (A.K.) used as an antioxidant. All these substances were used in a 1% dilution in soft paraffin. To avoid contamination they were transferred to the skin on the end of an orange stick, which was not used again. In addition, 31 patients were tested against monobenzyl ether of hydroquinone, which is used in the United States as an antioxidant under the name of agerite alba. Twenty-five patients were also tested against untreated latex.

Patch tests were read after 48 hours and again five or seven days after removal of the patches. After a few days' interval doubtful reactions were found to have faded (when they were regarded as negative) or to have become obviously positive.

Results of Patch Tests

When tested against household gloves, 37 patients gave positive and five gave negative reactions. Twenty-four patients were tested against their own gloves and a red household glove kept in the department for the purpose. Seven gave positive and five gave negative reactions to both specimens, while 12 gave a positive reaction to their own glove and a doubtful or negative one to the hospital glove.

All but two patients gave positive reactions to one or more of the accelerators against which they were tested. Forty-two tests against P.T.D. gave 30 positive reactions (71.43%) and against T.M.T. 20 positive reactions

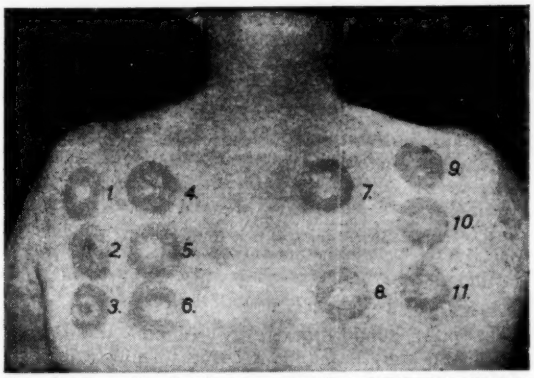

FIG. 6.—Case 14. Patch tests. Positive: P.T.D. (2); T.M.T. (3); own household glove (9). Negative: P.B.T. (1); Z.D.C. (4); M.B.T. (5); A.K. (6); hydroquinone (7); latex (8); hospital glove (10); surgical glove (11).

(47.62%). Against M.B.T. 42 tests gave 15 positive reactions (35.71%). Seventeen patients gave positive reactions to both P.T.D. and T.M.T. (Fig. 6), while 8 reacted to both M.B.T. and either P.T.D. or T.M.T. Only 2 out of 42 patients gave positive reactions to Z.D.C. Of 42 tests against P.B.T. there was only one positive reaction. Patients giving positive reactions to these substances also reacted to P.T.D., T.M.T., or M.B.T. Two patients gave positive reactions to their gloves but negative reactions to all the accelerators.

Twenty-five tests against untreated latex and 37 against the A.K. reaction powder were all negative.

Prognosis

Eczema or dermatitis of the hands is often slow to heal, and the rash did not invariably clear up as soon as the rubber gloves were discarded; a rapid improvement was, however, seen in nearly every case. when a questionary was sent to 27 patients who had been seen at least six months previously, 17 stated that the rash was cured and the remaining 10 that it had improved since they discarded their rubber gloves.

Discussion

The clinical picture of glove dermatitis is usually characteristic, but not invariably so, and patch tests should be done in every suspected case. Tests to glove material were not always reliable, and both false-positive and false-negative reactions were seen. Sidi and Huerre (1952) believe that all cases are not due to accelerators, and two patients in the present series gave positive reactions to their gloves but did not react to any of the accelerators against which they were tested. The remaining 40 reacted to one or more of the accelerators, sensitivity to P.T.D. being found in 71.43% of cases and to T.M.T. and M.B.T. in 47.62% and 35.71% respectively. It was felt, therefore, that tests against these accelerators were more reliable as evidence of rubber sensitivity than tests with patches of rubber glove, though the patient's own glove was more likely to give a positive reaction than a specimen glove which had been kept in the out-patient department for patch-testing. It has been suggested (Anderson, 1944) that patch tests may be positive on the backs of the hands but negative elsewhere. Generally speaking, however, sensitivity is not localized but rapidly spreads over the whole skin.

Vulcanization may continue at a slow rate for some weeks after manufacture, so that the longer the glove is kept the less amount of free accelerator is likely to remain on the surface. The products of the larger manufacturers are likely to be stored for about three months before reaching the shops, a fact which probably reduces the risk of their giving rise to dermatitis. Many of the antioxidants used in rubber manufacture possess both irritant and sensitizing properties (Mallette and Von Haam, 1952), and monobenzyl ether of hydroquinone is a common cause of rubber dermatitis in the United States (Blank and Miller, 1952; Gaul, 1957). It is, however, seldom used in this country as an antioxidant, and there were no positive reactions to it in the present series, nor to the amine-ketone reaction powder A.K. Untreated rubber latex appeared harmless and also gave no positive reactions in the present series, though it has been suggested (Sidi and Huerre, 1952; Thulliez, 1958) that some cases of dermatitis are due to sensitivity to the rubber itself.

Sensitivity to gloves may complicate an idiopathic eczema of the hands or a detergent dermatitis, and 13 out of 30 patients in the present series wore gloves because they had developed a rash on the hands. Gloves made from polyvinyl chloride are unlikely to sensitize, and should be worn in preference to rubber when the skin of the hands is inflamed.

Summary

Forty-two cases of rubber-glove dermatitis are described. The pattern of the rash is usually characteristic, but not invariably so. Untreated rubber latex appeared harmless, and in 40 cases dermatitis was due to accelerators, usually thiuram compounds or mercaptobenzthiazole. Patch tests with these chemicals were more reliable than tests with rubber material.

In two cases the cause of the dermatitis was unexplained. Thirteen out of 30 cases had a pre-existing hand eczema.

I am indebted to Dr. H. J. Stern for his advice regarding the chemistry of rubber and for supplying the formulae in Fig. 1, and to Mr. R. J. Reid, of the London Rubber Company, for information about the manufacture of rubber gloves. I am also indebted to Dr. F. R. Bettley and Dr. C. D. Calnan for permission to study their cases, and to the medical artist and photographic department of the Central Middlesex Hospital for assistance with the illustrations.

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MUSCLE PAINS THAT FOLLOW ADMINISTRATION OF SUXAMETHONIUM

BY

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Since Churchill-Davidson (1954) described a relationship between the administration of suxamethonium chloride and post-operative muscle pains, claims have been made for many methods of prevention. This paper describes an investigation of three such methods: (a) the use of the bromide salt of suxamethonium in fresh solution; (b) the administration of neostigmine and atropine after the return of normal respiration; and (c) the intravenous injection of a small dose of gallamine triethiodide prior to the suxamethonium in a group of out-patients. It also includes an assessment of the incidence of muscle pains in relation to age, sex, and site of operation after various surgical procedures in in-patients.

Method

The out-patients were an unselected group of patients who had bronchoscopy performed under general anaesthesia and who were sent home within four hours of the procedure. All received a questionary, one of the questions on which was: "Did you have any pain or weakness in your muscles the following day?" If the answer was in the affirmative, then a second questionary asking for more detailed information was sent (Churchill-Davidson, 1954).

The in-patients consisted of 289 consecutive patients who required intubation, which was performed after the administration of suxamethonium chloride. Anaesthesia was maintained with various inhalational agents.

The anaesthetic technique for all the out-patients was as follows.

Premedication.—Papaveretum hydrochloride, 10 mg., and hyoscine hydrobromide 0.425 mg., except for those patients over 60 years of age, who received atropine sulphate, 0.6 mg., instead of the hyoscine hydrobromide.

Anaesthesia.—Intravenous thiopentone, 200–500 mg., followed by a total dose of 60 to 225 mg. of suxamethonium. The larynx and trachea were sprayed with 4 ml. of 4% lignocaine and a No. 6EG oesophagogastric tube was placed in the trachea with its tip at the level of the carina. Through this, oxygen at a rate of 3 litres a minute was administered throughout the bronchoscopy.

Results

The inquiry into the incidence of pain after use of the different methods gave the following results.

(a) Suxamethonium Bromide ("Brevidil M") Made up in Normal Saline Before Each Day's Cases

	No.	With Pain	Without Pain
Out-patients	32	59%	41%

These figures agree with Churchill-Davidson's results for this procedure using a similar technique with suxamethonium chloride.

(b) Atropine, 1 mg., and Neostigmine, 1 mg., Intravenously on the Return of Respiration

	No.	With Pain	Without Pain
Out-patients	64	55%	45%
In-patients	116	19%	81%

All the in-patients had a non-depolarizing relaxant after the initial return of respiration and prior to the injection of neostigmine.

These figures are not significantly different from those in section (*a*) or in the total of in-patients.

(c) Gallamine Triethiodide, 40 mg. Intravenously, Before Suxamethonium Chloride

	No.	With Pain	Without Pain
Out-patients	7	28%	72%

Gallamine Triethiodide, 20 mg. Intravenously, Before Suxamethonium Chloride

	No.	With Pain	Without Pain
Out-patients	38	36·8%	63·2%

The prior administration of gallamine triethiodide does significantly lower the incidence of muscle pains.

Of the 289 in-patients who received suxamethonium chloride 23.6% had pain and 76.4% had no pain.

Effect of Age, In-patients

	No.	With Pain	Without Pain
Below 27 years (average 21)	36	16·7%	83·3%
Over 63 years	63	12·7%	87·3%
„ 70 „	12	Nil	100%

There were no patients at the extremes of age in the out-patient series. These figures show a reduction in the incidence of pain with increasing age.

Discussion

This investigation confirms the high incidence of muscle pains after the administration of relatively large doses of suxamethonium that has been reported by all workers who have investigated this common and often distressing complication of anaesthesia, and bears out the difference found between out-patients and in-patients (Churchill-Davidson, 1954; Hegarty, 1956).

In spite of the claim of Ruddell (1957), it was found that the use of a fresh solution of suxamethonium bromide had no effect on the incidence of muscle pains, and this is in agreement with the results of Leatherdale and his co-workers (1959). König (1956) found that the intramuscular injection of neostigmine, 0.5 mg., three-quarters to one hour after the examination, reduced the incidence of pains after bronchoscopy from 57% to 30%. But the present investigation failed to demonstrate any decrease in the incidence of pains when neostigmine was administered intravenously a few minutes after the bronchoscopy. This may be due to the failure of the motor end-plates to have returned to normal and to the fact that neostigmine produces a degree of neuromuscular block itself (Churchill-Davidson and Christie, 1959).

Of the methods used in this investigation in an attempt to reduce the incidence of muscle pains, only the prior injection of gallamine triethiodide shows a statistically significant improvement. Morris and Dunn (1957) found that, of the methods they tried, only the prior injection of 5 mg. of D-tubocurarine was effective.

The use of a non-depolarizing relaxant prior to the administration of a depolarizing agent, however, is not without danger: larger doses of the depolarizing agents are required to produce similar conditions to those obtaining when a non-depolarizing agent is not used, and difficulty may be experienced in the establishment of normal respiration particularly in patients for bronchoscopy.

In four of the seven patients who received gallamine triethiodide, 40 mg., prior to the suxamethonium chloride, respiration did not return as rapidly as was expected, and in one patient respiration was inadequate and required assistance for 10 minutes after the bronchoscopy had ended, and was adjudged to be adequate only after an intravenous injection of edrophonium, 10 mg., followed by neostigmine, 2.5 mg. This led to the abandonment of the use of such large doses of gallamine as 40 mg. The same criticisms can be applied to the use of 20 mg. of gallamine triethiodide, and, indeed, in one of these patients an injection of edrophonium, 10 mg., was required to return respiration to normal.

Hegarty (1956) noted a sex difference in the incidence of muscle pains, and this was confirmed by Leatherdale and his co-workers. The results of this investigation do not agree with their findings (see Table I). The difference in the out-patient series is not significant, though it is in the same direction, but the trend in the in-patients is in the reverse direction. This may be because the in-patients are unselected and other factors, such as age and site of operation, may be intervening.

TABLE I.—*Effect of Sex on Incidence of Muscle Pains*

	Sex	No.	With Pain	Without Pain
Out-patients:				
Suxamethonium bromide ..	M	27	59%	41%
	F	5	60%	40%
Atropine and neostigmine ..	M	59	51%	49%
	F	5	100%	Nil
Gallamine triethiodide 40 mg. ..	M	5	20%	80%
	F	2	50%	50%
,, ,, 20 ,, ..	M	31	35·5%	64·5%
	F	7	43%	57%
Total	M	122	47·5%	52·5%
	F	19	63%	47%
In-patients	M	69	32%	68%
	F	220	21%	79%

Jackson Rees (1958, personal communication) and Ruddell (1959) state that post-operative muscle pains do not occur in children after the use of suxamethonium. The number of children in this series does not allow an accurate assessment of the incidence of pain, but in those below the age of 27 the incidence is low, but not significantly so. On the other hand, the incidence of post-operative muscle pain is significantly less in those over 60 years of age.

The incidence of muscle pains in relation to different operations is of interest (see Table II). Previous reports have been confined mainly to operations about the head and neck.

This investigation shows that a very high incidence occurs after investigational procedures and a low incidence after thoracotomy and upper abdominal operations, in the former the absence, and in the latter the severity, of the post-operative pain may be accentuated, and may mask the severity of the muscle pains due to suxamethonium.

TABLE II.—*Analysis of Results in In-patients in Relation to Sex and Site of Operation*

Operation	Total No. Patients	With Pain		Without Pain		% of Total with Pain
		M	F	M	F	
Aortogram and air encephalogram ..	13	8	3	1	1	85
Thoracotomy ..	17	1	—	2	14	5·9
Upper abdominal ..	27	—	1	10	16	3·7
Lower ,, ..	90	—	22	13	55	24·4
Extremities ..	20	3	3	5	9	30
Remainder ..	122	10	17	16	79	22
Total	289	22	46	47	174	23·5

The muscle pains that follow the administration of suxamethonium are a common complication of modern anaesthesia. Their incidence is related to age and to whether the patient is kept in hospital or sent home after the operation. This is probably equivalent to saying that the incidence is less if the patient rests after the procedure. The incidence can be reduced by the prior administration of non-depolarizing muscle relaxants, but this practice is not recommended.

Summary

The administration of suxamethonium bromide instead of suxamethonium chloride has no effect on the incidence of post-operative muscle pains in a group of out-patients.

The intravenous injection of atropine and neostigmine at the end of the bronchoscopy has no effect on the incidence of muscle pains.

Gallamine triethiodide administered intravenously beforehand in a dose of 20 mg. lowers the incidence and severity of the pains but is liable—particularly in patients for bronchoscopy—to cause respiratory difficulties at the termination of the bronchoscopy.

After the administration of suxamethonium chloride to in-patients, nearly a quarter suffer from post-operative muscle pains, the incidence being less at the extremes of age and after certain operations.

Every time suxamethonium is used consideration must be given to the indications for its use and the incidence of muscle pains afterwards, and we must all hope that the chemists will produce a new relaxant with the advantages of suxamethonium but without its capacity for producing these pains.

My thanks are due to May & Baker Ltd. for generous supplies of "brevidil M," to Dr. H. C. Churchill-Davidson for his constant encouragement throughout this work, to Dr. W. D. Wylie for help with the preparation of the manuscript, and to Miss J. F. Davenport for secretarial assistance.

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Over a million tons of smoke are emitted yearly from domestic fires, compared with half a million tons from industry and 100,000 from the railways. On the other hand, domestic chimneys contribute only 100,000 tons out of the 900,000 tons of grit and dust that are emitted. These are the two main forms of pollution with which the Clean Air Act is concerned. Sulphur dioxide gas, given off from all solid fuels and fuel oils, totals 5½ million tons, to which domestic fires contribute nearly a million tons. These are a few of the many facts about air pollution and the campaign for its prevention contained in the *Clean Air Year Book, 1960*, published by the National Society for Clean Air at 2s.

GRANULOSA-CELL TUMOURS CAUSING PRECOCIOUS PUBERTY

OESTROGEN FRACTIONATIONS IN TWO PATIENTS

BY

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A review of the literature in 1955 revealed 62 cases of precocious puberty associated with granulosa-cell tumour (Pedowitz *et al.*, 1955). Oestrogenic activity of the urine had been assayed biologically in some of these cases and found to be greatly raised.

We report three further cases of precocious puberty caused by granulosa-cell tumour, in two of which both urinary and tumour oestrogens were fractionated and assayed biochemically. So far as we are aware, this is the first report of quantitative biochemical oestrogen estimation in this condition.

Case 1

A coloured girl aged 2 years presented with a two-months history of progressive enlargement of the breasts and growth of pubic and axillary hair (Fig. 1). For two weeks before admission she had had intermittent vaginal bleeding, which varied in intensity. The breasts were lumpy—resembling fibro-adenosis, though a biopsy was not done to confirm this.

FIG. 1.—Case 1. Demonstrating advanced breast development and large abdomen.

The labia majora, labia minora, and clitoris were well developed and approached adult proportions. The mons veneris and labia majora were covered with a moderate growth of hair. There was a firm mobile abdominal mass arising from the left fornix. The uterus and cervix were enlarged. Bone age was consistent with chronological age. An *x*-ray film of the skull was normal.

At operation a circumscribed ovarian tumour about 2 in. (5 cm.) in diameter was removed from the left side. The uterus measured 2 by 1½ by ¾ in. (5 by 3.2 by 1.9 cm.).

Pathology.—The cut surface of the ovary consisted of yellow cellular tissue with several cysts, interspersed with fibrous bands (Fig. 2). Histological examination revealed masses of granulosa cells with little rosette arrangement, divided into islands by connective-tissue stroma. Mitotic figures were fairly numerous, and there were thin-walled vessels between the tumour cells, though without obvious vascular invasion. At one edge several follicular cysts were seen.

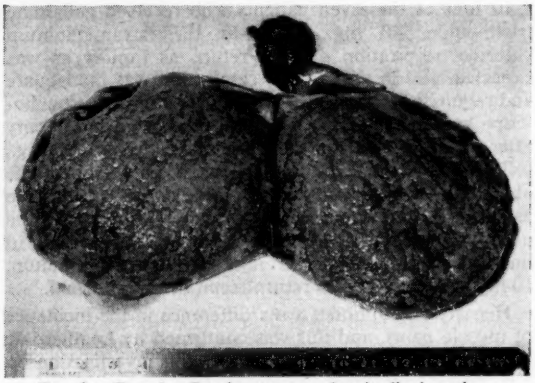

FIG. 2.—Case 1. Ovarian tumour, longitudinal section.

Intermittent vaginal bleeding persisted for eight days and was more severe than pre-operatively. Six months after the operation there had been no regression of the signs of puberty.

Case 2

An African girl aged 3 years had a history of progressive growth of breasts and pubic hair for eight months before admission. In addition there had been slight vaginal bleeding, of variable intensity, for the same period. The clinical picture was very similar to that of Case 1. There was a right-sided ovarian tumour about 2½ in. (6.4 cm.) in diameter, easily palpated abdominally. The perineum, however, was not as well developed as in Case 1, and was that of a prepubertal child. The clitoris was normal in size for the age of the child. The uterus was enlarged, but not to the same extent as in Case 1. The bone age was assessed at 4 years. *X*-ray examination of the skull revealed no abnormality.

FIG. 3.—Case 2.

Operation revealed a right-sided solid ovarian tumour, about 3 in. (7.5 cm.) in diameter, yellow in colour and with large areas of cystic change. The other ovary was quite normal. There was no evidence of spread. The uterus measured 1½ by 1 by ¾ in. (3.8 by 2.5 by 1.9 cm.).

Pathology.—Macroscopically the ovary resembled that in Case 1. Microscopical sections showed a granulosa-cell tumour of the ovary in which there were fairly large areas of necrosis and areas that had undergone luteinization. The cell arrangement conformed to the diffuse type, without rosette formation. Very few mitotic figures were evident, and it was not possible to assess the degree of malignancy. A few cystic areas were seen.

On the third post-operative day the patient developed slight vaginal bleeding, which persisted for four days. Eight months after operation there was no change in the amount of pubic hair nor in the size of the breasts or uterus.

Case 3

An African girl aged 2 years 4 months presented with a history of growth of breasts and pubic hair and slight

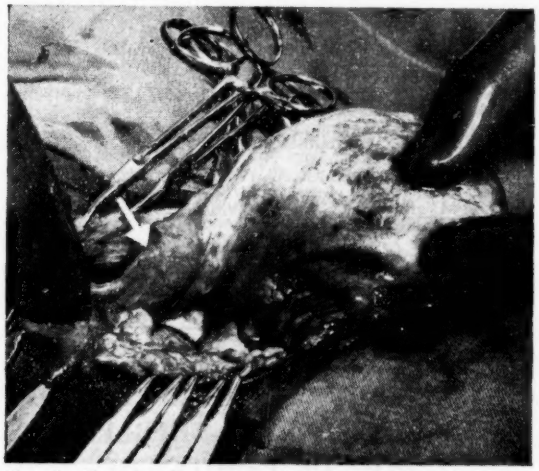

FIG. 4.—Case 2. Appearance of tumour at operation (uterus indicated by arrow).

vaginal bleeding at regular intervals for several months. A right-sided ovarian tumour was easily palpated abdominally; it was about 2 in. (5 cm.) in diameter. The perineum was that of a child, with minimal development of the clitoris and labia minora.

At operation there was a localized solid yellow right-sided ovarian tumour about 1¼ in. (3.2 cm.) in diameter. The uterus was about the same size as in Case 2. No pathological report is available, the patient having been treated in a country hospital.

FIG. 5.—Case 3.

Slight vaginal bleeding was noted on the second and third post-operative days. There was no change in the features of precocious puberty after two months.

Endocrine Investigations

Methods. — The tumours were ground and the oestrogens extracted in ether and acetone. The quantitative biochemical estimation of individual oestrogen fractions, as described by Brown (1955), was applied to both the extract and the urine. In Case 1 stilboestrol was given in doses of 1 mg. three times daily for four days, and the urinary oestrogen estimated on the third and fourth days. Gonadotrophic hormone in the urine ("F.S.H.") was assessed by a rat ovarian method, after extraction with kaolin (Albert, 1956). Urinary 17-ketosteroid and 17-hydroxycorticoid levels were assayed by the methods of Norymberski *et al.* (1953) and Appleby *et al.* (1954).

Results.—Twenty-four-hour urinary oestrogen estimations in Cases 1 and 2 are recorded in Table I, and compared with those of two control children. The total oestrogens in each case were much higher than in the normal children, but by far the greatest fraction was made up of oestriol, while oestradiol was no higher (even lower in Case 2) than in the normals. Stilboestrol as administered produced no appreciable change in urinary oestrogen output. There was a gratifying post-operative fall in urinary oestriol in both cases, though the oestrone appeared to rise in Case 2. The oestrogen content of the tumour extracts (Table II) were remarkably low. The smaller tumour contained far more oestrogen. The urinary gonadotrophins (F.S.H., Table III) were raised to within the adult range in both cases, with a fall in the level after operation in Case 2. (They were not measured post-operatively in Case 1.) The urinary 17-ketosteroid and hydroxycorticoid (Table III) levels were not abnormal.

TABLE I.—*Urinary Oestrogen Excretions in μg. per 24 Hours*

	Oestradiol	Oestrone	Oestriol	Total Oestrogen
Controls:				
1. Girl, aged 4½ years ..	1·7	2·1	4·0	7·8
2. ,, ,, 3½ ,, ..	2·4	2·0	1·4	5·8
Case 1:				
Pre-operative	2·3	3·7	15·1	21·1
After 9 mg. stilboestrol ..	2·6	3·5	15·3	21·4
,, 12 ,, ,, ..	1·8	2·9	13·1	17·8
11 days post-operatively	0·4	0·4	5·1	5·9
Case 2:				
Pre-operative	0·6	0·9	18·0	19·5
6 days post-operatively ..	0·6	0·0	8·4	9·0
14 ,, ,, ..	0·3	2·4	0·7	3·4
6 months ,, ..	0·3	3·1	3·4	6·5

The sensitivity of the method probably does not go below 2 μg. of oestrogen.

TABLE II.—*Oestrogens Extracted From Tumours*

Case No.	Amount of Tumour Extracted	Oestradiol	Oestrone	Oestriol	Total Oestrogen
1	11·4 g.	1·8 μg.	9·5 μg.	2·6 μg.	13·9 μg.
2	63 g.	0·9 ,,	0·6 ,,	0·6 ,,	2·1 ,,

TABLE III.—*Urinary Gonadotrophins, 17-Ketosteroids, and Hydroxycorticoid Excretions*

	F.S.H. (r.o.u.)	17-Ketosteroids (mg./24 hrs.)	17-OH-corticoids (mg./24 hrs.)
Normal for age	0 (Albert, 1956)		
Young adult normal ..	±14*		
Case 1:			
Pre-operative	14†	1·8	2·0
10 days post-operative	—	1·2	5·0
Case 2:			
Pre-operative	12	2·0	7·0
Post-operative	3‡	—	—

* This is a rough mean of Albert's normals, and tallies with our own experience in over 30 normal subjects.
† 100% increase in rat ovarian weight over control.
‡ No significant increase in rat ovarian weight.

Discussion

There is a good correlation between the severity of the clinical findings and the level of total oestrogen secretion in Cases 1 and 2. Case 1, though younger, had more advanced pubertal changes than Case 2, and histology of the tumour also showed more active mitosis. The excretion of both oestradiol and oestrone—the two most potent oestrogen fractions—was much higher than in Case 2. Also there was apparently more oestrogen in the tumour of Case 1.

The level of the total urinary oestrogens and the individual fractions was no higher than we find in adult females around mid-cycle—in fact, not as high. In cases reported in the literature the oestrogen levels when assayed biologically have been found to be much higher in cases with granulosa-cell tumour than in adults with

normal ovulatory cycles (Pedowitz *et al.*, 1955). The comparatively low levels obtained with the chemical method in our cases suggest that the most active oestrogens produced by granulosa-cell tumours may not appear in the urine as oestradiol, oestrone, or oestriol. Furthermore, the low level of oestrogen found in the tumours could also be explained if they are producing a potent oestrogen, not measured by Brown's techniques. It is known that there *are* other oestrogens in normal urine and ovaries, though their importance is usually less than the three measurable fractions (Brown *et al.*, 1959).

Estimation of urinary oestrogens may be important both diagnostically and prognostically. After removal of the tumour urinary oestrogens should return to normal levels. In both these cases there was a marked decrease in the oestrogen levels in all three fractions by the second week. In Case 2 the oestrogen level had risen again six months post-operatively.* In any event, since there has been no clinical regression in signs in either child we feel that both should have regular clinical examinations and urinary oestrogen assays. A tendency of the latter to rise further would be an indication to re-examine the remaining ovary, since bilateral tumours, though uncommon, do occur, and the second tumour may be so small as to be missed at the first laparotomy. In most cases reported in the literature, a distinct regression in pubertal signs takes place fairly rapidly after removal of the tumour in younger patients (Anderson and Sheldon, 1937 ; Gross, 1940 ; Fuller and Smith, 1941 ; Haines and Jackson, 1950).

We were surprised to find elevated " F.S.H." levels, since granulosa-cell tumours are presumed to be autonomous. This finding has been reported in three other cases in the literature (according to Pedowitz *et al.*, 1955). In an attempt to see if any of the oestrogen secretion was under pituitary control, we gave stilboestrol for four days, hoping thereby to suppress any pituitary over-activity. If oestrogen production was in fact under pituitary control, this should also have been depressed. The oestrogen excretion, however, was not affected. The high " F.S.H." levels would appear to indicate either that the tumours are under some pituitary control (which the above-mentioned observation does not completely exclude) or that the tumours themselves produce a substance capable of increasing the size of rat ovaries.

Summary

Three cases of precocious puberty due to granulosa-cell tumours in infancy are described, together with biochemical estimation and fractionation of both urinary and tumour oestrogen content in two of them.

It is suggested that the tumours may produce a potent oestrogen which is not measured by the current chemical methods, and may also produce a gonadotrophic substance.

We thank Professor F. Ford and Dr. J. Hansen, of the Department of Paediatrics of the Red Cross War Memorial Hospital, Capetown, for their encouragement and assistance in undertaking these studies. Miss T. Gebbardt performed the oestrogen estimations. Surgery was performed by Professor J. F. Louw and Mr. van der Riet. We thank Dr. D. MacKenzie for the pathological reports.

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*This rise is probably not significant, since the levels are not elevated above those found in our two controls.

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ST. ANTHONY'S FIRE REKINDLED: GANGRENE DUE TO THERAPEUTIC DOSE OF ERGOTAMINE

BY

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In the tenth and eleventh centuries ergot-poisoning from rye infected with *Claviceps purpurea* was a common epidemic disease in France, and was known by a number of names, such as mal des ardents, ignis sacer, and feu sacré. The emphasis on fire is explained by the violent burning pain in the limbs ; sufferers unable to bear the heat in their beds sought relief in the open air. With the onset of gangrene the blackened limbs were likened to charcoal. Several houses of the Order of St. Anthony were devoted to the care of sufferers from the holy fire, and the walls of their hospitals were painted a symbolic red or flame colour. It seems beyond reasonable doubt that St. Anthony's fire originally referred to gangrenous ergotism. However, the definition of St. Anthony's fire in many dictionaries and encyclopaedias mentions erysipelas. The patient whose case is described below presented with such a remarkably red face that we felt this might have accounted for the confusion with erysipelas and other infectious skin diseases.

The literature reveals a large number of cases of ergotism in both Great Britain and America, resulting from either liquid ergot or ergotamine tartrate, despite the fact that contraindications to the use of ergotamine are well documented. They were recently summarized by Greene (1959), and include peripheral vascular disease, hypertension, and coronary disease ; pregnancy ; thyrotoxicosis ; gross sepsis ; hepatic and renal disease ; and anaemia. In the *British Medical Journal* (1959), under " Notes and Comments," the expert writes: " In those persons who are sensitive its [ergotamine] use has produced nothing less than disaster. Whenever a new case is reported it becomes a matter for astonishment that responsible manufacturers make it for medical use."

That serious ergotism can occur from normally accepted therapeutic doses of ergotamine in the absence of known contraindications was forcibly impressed on us recently.

Case Report

A married woman of 45 was admitted to hospital on February 22, 1959, as a medical emergency, complaining of intense pain in the legs and arms. Her doctor had been unable to feel her radial pulses or record her blood-pressure. Thinking she had developed profound peripheral circulatory collapse, he had given her 100 mg. of hydrocortisone intramuscularly.

On examination she was fully conscious, somewhat agitated, and in severe pain. Temperature was 101° F. (38.3° C.), the face and neck were sweating and flushed to a fiery red. All four extremities were cold and mottled blue and white. Pulsation could just be felt in the femoral and subclavian arteries, but there were no pulses distal to these vessels. Blood-pressure was not recordable in any limb. The carotid pulses, however, were strikingly forceful and the aortic second sound was very loud. The heart rate and rhythm were normal and the electrocardiogram showed no abnormality. There were hyperalgesia on tendon pressure, dysaesthesia to pin-prick, but normal appreciation of light touch in all limbs. Tendon jerks were depressed in the lower but brisk in the upper limbs. The fundi were healthy. There was proteinuria (0.5 g./l.), W.B.C. 16,500/c.mm., and Hb 89% (13.34 g./100 ml.).

In view of the intense flushing of the face, bounding carotid pulses, and loud aortic second sound it was felt that the blood-pressure in the head and neck was probably high and the failure to record it in the limbs due to intense arterial spasm. The clinical features suggested the probability of ergotism.

There was nothing in her previous history to suggest any vascular disease or undue sensitivity. A week before admission she had developed mild influenza, which was then prevalent. Recently her menstrual periods had been rather erratic and a little heavier. The last one began on February 20. Further inquiry revealed that her practitioner had prescribed 1 mg. of ergotamine tartrate t.i.d. orally with a view to modifying the loss. In all, she had taken seven tablets from February 20 until her admission on the 22nd.

On February 20 she had vomited several times throughout the day and experienced considerable abdominal pain. There was no further vomiting and the pain settled. The same day, however, cramplike pains developed in both lower limbs. These persisted, and by the 22nd the forearms and hands were also affected. By then the pain was exceedingly severe in all four limbs, and her husband noticed that her feet and legs were white and very cold to touch. He applied hot-water bottles to them in an attempt to give her relief. During February 22 patchy cyanosis appeared, and because of the coldness, pain and general malaise, her doctor was recalled and he arranged her admission to hospital at once.

She had vomited after taking the first two tablets. It was the day after the drug was first taken and after consuming only two or possibly three tablets, that the legs and feet first became cold. Several of the remaining tablets were sent for assay and found to contain the stated 1-mg. quantity of ergotamine tartrate.

Management

It was anticipated that the spasm would soon wear off, and therefore only symptomatic measures for the pain were adopted, along with exposure of the limbs to room temperature and warming of the trunk. Next day, however, the ischaemia was worse. There was progressive sensory loss and the deep reflexes in the legs disappeared. The calf muscles were bunched and intensely painful. The small muscles of the hands were paralysed. Accordingly heparin was injected intramuscularly owing to the absence of accessible veins, and phenindione was given orally. Tolazoline, 50 mg., was injected into the left femoral artery just distal to the inguinal ligament. Within four minutes there was a pronounced flushing over the upper two-thirds of the thigh extending up over the lower abdomen, but no change in the ischaemic leg and foot could be detected. The same dose of tolazoline, with 5,000 units of heparin, was injected into the right femoral artery with no better result. Intra-arterial "hydergine" (0.03 mg.) was also ineffective.

Sympathetic block, intra-arterial procaine, other vasodilators, and more active cooling of the ischaemic extremities were all considered, but were rejected for reasons given later.

The skin colour and temperature gradually improved in the upper limbs. On February 25, some 40 hours after admission, the fingers of the left hand were blue, but the rest of the hand was quite pink. The right hand was still cyanosed, and it was clear that the thenar muscles were infarcted. In the legs a line of demarcation appeared at the junction of the middle and upper thirds of the calf. By now the brachial and popliteal pulses were easily felt, and the femoral pulsation was strong. The distal pulses were still absent. Blood-pressure could now be recorded, and the first reading was 200/100 mm. Hg. By February 26 the left radial pulse had returned and there was striking improvement in the left hand overnight. Light touch could now be appreciated in the hands, excepting the right thumb and index finger. Movements in the left hand were good, though some contracture remained. On the right side, flexion contracture of fingers was present (see Fig. 1,b).

On February 27, five days from admission, the right radial pulse had returned. Pulsation of the digital arteries of the left hand and the right middle, ring, and little finger was first noticed on March 3, but may have returned earlier. Sharp lines of demarcation indicated that maximum improvement had occurred, and that amputation was advisable. The patient was transferred from the medical unit on March 7, when her general condition was good, blood-pressure had fallen to 165/100 mm. Hg, and proteinuria had disappeared. Amputation of both legs, the right thumb, and tip of the right index finger was performed. (Fig. 2 summarizes the main features of the illness.)

The blood-flow in the left hand was measured by venous occlusion plethysmography on April 22. This reached 11 ml./100 ml. of tissue/minute during indirect heating; normally it should have risen to at least 30 ml. Vasomotor control was present, since the flow fell to 2 ml./100 ml. of tissue/minute within a quarter of a minute of the application of a cold wet towel to the thighs.

An attempt was made to exclude subclinical disease such as might predispose to undue sensitivity to ergotamine. Liver-function tests were normal. Renal-function tests showed normal blood urea and intravenous pyelogram, but a reduction creatinine clearance averaging 75 l./24 hours.

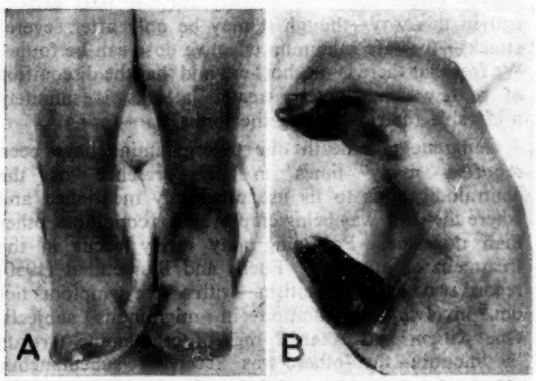

FIG. 1.—(*a*) Five days after admission, and seven days from taking the first 1-mg. tablet of ergotamine tartrate. Maximum improvement had occurred. (*b*) Shows right thumb and forefinger—same time interval.

This reduction in glomerular filtration might, however, have resulted from the vasoconstriction, and this is supported by a known blood-pressure record of 140/80 in October, 1958, whereas the pressure throughout convalescence remained not less than 180/100 mm. Hg. In any event, the renal defect seemed insufficient to account for an undue sensitivity to the drug.

Examination of the amputated parts revealed no arterial disease, though many of the vessels contained clot.

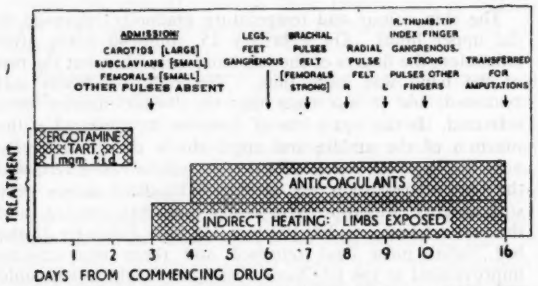

FIG. 2.—Ergotamine tartrate, 7 mg. by mouth over three days. Summary of main developments.

Discussion

The course of this illness put the diagnosis of gangrenous ergotism beyond all reasonable doubt. Proteinuria may result from renal vasoconstriction. Fever (Githens, 1917) and leucocytosis (Pajevic, 1933) are also known effects of ergot.

In the present case disaster seems to have resulted from an excessive response to standard dosage of ergotamine tartrate. Though it is true that thousands of persons throughout the world take ergotamine preparations for migraine with no serious consequence and considerable benefit, such an eventuality may arise at any time. Unfortunately the dose which is effective in relieving the headache often produces nausea, vomiting, muscle cramps, and paraesthesiae. It is commonly recommended, however, that 1 to 6 mg. can be taken as an initial dose. The margin between an adequate and a dangerous dose may thus be extremely narrow. Therefore we consider it is important to prescribe 1 mg. orally in the first instance. If this gives insufficient benefit, 2 mg. can be given in the next attack provided no serious side-effects have been noticed. If these are non-existent or mild, the patient can take a slightly larger dose immediately for the next attack, and in this way—though it may be only after several attacks—the safe minimum effective dose can be found. We feel that there is no short-cut and that the discomfort of a few inadequately treated attacks is infinitely preferable to endangering the limbs.

Gangrene and death due to ergotamine have been reported many times in the presence of the contraindications to its use previously mentioned and where the drug was being employed for conditions other than migraine. Poisoning may rarely occur in the treatment of migraine. Fuchs and Blumenthal (1950) record two cases of ergotism—with severe symptoms but not involving amputation—in migrainous subjects. One patient had taken 2 mg. of ergotamine tartrate by mouth; the other was receiving subcutaneous dihydroergotamine, up to 1 ml. per injection.

Judging from the course of the present case, spasm of the limb vessels may be so severe that no vasodilator drugs can reach the affected parts. It is possible that vasodilators may be effective if they are given intra-arterially earlier and before occlusion is complete. There is no specific antidote. Sympathetic-nerve block has been suggested, but there are reasons why this should not be done. Firstly, vasodilator as well as vasoconstrictor nerves would be paralysed, whereas heating of the body results in complete release of vasoconstrictor tone with activation of vasodilator fibres in the upper limb. Unfortunately, vasodilatation in the feet in response to body-warming may be much less (Pickering and Hess, 1933). Secondily, Von Storch (1940) quotes Polak as showing that gangrene is actually hastened by section of the abdominal sympathetic chains. Also, Bluntschli and Goetz (1948), studying the circulatory effects of dihydrocornine and dihydroergotamine in sympathectomized and non-sympathectomized patients, conclude that the effect of both these drugs on the sympathectomized limb is invariably vasoconstriction. Pichler *et al.* (1956) found that intense constriction occurred in isolated cranial-artery segments placed in a suspension of ergotamine tartrate, and concluded that the effect of the drug is entirely peripheral on the vessel wall.

Summary

A case of gangrene due to ergotamine tartrate in dosage well within the accepted therapeutic range is described and the potential dangers of ergot preparations are emphasized.

The ineffectiveness of treatment once intense spasm has occurred is discussed.

The importance of a gradual approach towards finding the minimum effective dose of ergotamine in each patient is stressed.

The patient was convalescent from influenza and was being treated for menorrhagia.

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The National Association for the Paralysed has assembled a collection of leaflets giving information about various aids, appliances, and gadgets, either manufactured in this country or easily made, which can help to overcome the everyday problems of disabled people. There are leaflets on aids in lifting; dressing aids for men and women; aids in the toilet; aids in the bathroom; recreational aids; planning and adaptation of living accommodation; aids in catering and drinking; aids in domestic work; aids in transport; aids to mobility; and aids for men and women with bladder weakness and incontinence. The cost is 10s. 6d. for a bound set of eleven, or 1s. for each leaflet, from the National Association for the Paralysed, 1, York Street, Baker Street, London, W.1.

USE OF PHENOL IN RELIEF OF SPASTICITY

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Maher (1955, 1957) drew attention to the remarkable effects of the intrathecal, subdural, and extradural injections of special solutions of phenol in the relief of pain, principally in cases of inoperable carcinoma. A surprising and interesting feature of these clinical experiments lay in the fact that very little additional neurological deficit was produced by these techniques, a phenomenon which Maher justifiably attributed to a selective action of the phenol upon pain fibres. Following up Maher's work, Nathan and Scott (1958) were able to show the relative safety of this method, particularly when using phenol in "myodil," though they commented on certain dangers they encountered in the use of a combination of silver nitrate and phenol. Brown (1958) also showed the value of solutions of phenol in glycerin and in myodil in the relief of pain, and alluded to the use of phenol in myodil for the amelioration of flexor and extensor spasms in three cases. Brown found no relief in two of these cases, and though there was relief in the third case the bladder became hypotonic. Maher (1955) had also alluded to the complication of retention occurring in his painful cases, particularly when he made his injections at a low vertebral level in order to relieve rectal pain, though his experience was that the retention cleared in three to four weeks.

The theoretical attractions of this method for the relief of spasticity and especially of the painful flexor and extensor spasms are obvious. Whatever one's views may be about the physiological mechanisms of postural tone, the clinical phenomena of spasticity must be attributable to a disturbance of the normal neural balance of the anterior horn cell. The pathological interruption of upper motor neurone pathways seemingly results in excessive activity of the afferent–efferent reflex arc. Pain transmission through the cord is still relatively unimpaired, and so one has the progression from spasticity to extensor and flexor spasms with associated pain. The functional defect in power in a case of spastic paraplegia is due in part to the interruption of upper motor neurone pathways and in part to the excess of stretch reflex activity in the lower motor neurones. Previous surgical attempts at anterior or posterior root section had stemmed from the acceptance of this theory but suffered from difficulties of technique and also from the fact that they resulted in a substantial increase in the existing neurological deficit.

With the advent of the knowledge that phenol solutions were capable of *selective* interference with pain transmission without noticeably adding to motor or other sensory deficit one naturally looked to this technique as a means of symptomatic relief for spasticity and especially for painful spasms. Consequently we began to carry out tentative experiments with intrathecal phenol in patients for whom there seemed little other hope of clinical aid. It was only after some months, when we began to compare our experiences, that the details of the most effective and least dangerous technique finally emerged.

Technical Considerations

Solutions to be Used.—It soon became apparent to us that the combination of phenol in myodil was much less efficacious than that of phenol in glycerin. This was attributed partly to the fact that phenol is released more slowly from the myodil and partly to the fact that the glycerin–phenol mixture tends to be absorbed directly on to the neural roots, whereas the myodil tends to remain in globular emulsive form. As to the strength of the solution, we found that 5% phenol in glycerin was both safe and effective provided that careful attention was paid to the positioning of the patient. Weaker solutions appeared to produce effects of shorter duration, but in certain cases a 2% solution may be satisfactory, and we often use this in ambulant cases. The most suitable quantity to be injected at each session was again found by trial and error to be of the order of 1 ml., though quantities from 0.5 to 1.5 ml. have been given. The technique of preparation of the glycerin–phenol solution is as follows:

Phenol	...	...	5 g. (or 2 g.)
Glycerin	...	...	to 100 g.

The glycerin is dried for one hour at 120° C. and transferred to a dry stoppered flask. The phenol is added and the flask shaken until solution is complete. The solution is then filtered through filter paper and filled into *dried* 2-ml. ampoules. The use of rubber tubing and bungs at any stage of the process is undesirable, because rubber selectively absorbs phenol. "Polythene" tubing has been found satisfactory for the filling process. The ampoules are finally sealed and sterilized at 150° C. for one hour.

Anatomical Factors.—At first sight the anatomical considerations might appear to be simple and straightforward; for patients with excessive extensor thrust interruption of the L 2/3 roots might reasonably be regarded as effective. Similarly, adductor spasm should theoretically respond to phenolization at these levels. If, on the other hand, flexor spasms predominate, chemical denervation at L 4/5 and S 1 seems the correct anatomical line of approach. These simple considerations, however, are complicated and conditioned by certain other factors. As hinted above, the principal danger lies in the affection of urinary bladder and sphincter action, with a resultant retention, and we have found that if phenolization reaches the cord itself (at L 1) or descends to the sacral roots, then this particular complication is very likely to occur. Moreover, though one aims to restrict the phenolization to two or at the most three roots, there tends to be some spread of effect to segments above and below the point of insertion. We have therefore now come to the realization that the maximum safe efficiency results from injections either at L 2/3 or L 3/4 intervertebral spaces, though occasionally the L 4/5 space has been used.

Technique

The technique of injection has now been evolved into a fairly rigid discipline. The patient is placed in the usual lateral position for lumbar puncture, and pillows are adjusted under the buttocks and trunk in such a way as to ensure that the appropriate intervertebral space is at the bottom of the putative watershed so

produced. Lumbar puncture is performed in the usual way in the space selected, an attempt being made, however, to direct the needle-point as far laterally as may be compatible with penetration of the theca. If, as the needle enters the theca, the patient complains of root paraesthesiae on the correct side the insertion is considered to be at its best. 0.2 ml. of a 5% solution of phenol in glycerin is injected slowly into the theca. (It is helpful to warm the solution to facilitate flow.) Patients are asked to comment on any sensation they may feel. Within 15 to 20 seconds they will usually say that they have a warm tingling in the region of the knee and thigh. Injection of a further 0.8 ml. of the solution over the space of 30 seconds then follows. If the initial paraesthesiae are in the buttock or ankle we advise discontinuance of the procedure, with a further attempt next day one space higher. Persistence of the injection in the face of such localization of the induced paraesthesiae almost invariably results in some bladder dysfunction. It will be found that within 60 seconds the injection has reduced tone in the leg.

Patients often complain of numbness and tingling, and for two to three hours there may be some motor affection, though in certain cases abolition of the spasticity may allow them to move a limb previously immobile. This motor deficit usually clears by the day after, and any objective sensory findings will similarly disappear. It is our practice to leave the patients for 15 minutes in the position in which the puncture is made. They are then allowed to lie on their backs with the head raised on two pillows for one hour. After that, full movement in or out of bed is permitted and indeed encouraged. The technique is repeated two days later on the opposite side, and we have given as many as six separate intrathecal injections to one patient in covering two intervertebral levels on each side.

Effect on Cerebrospinal Fluid

We had thought it likely that the introduction of phenol into the theca would result in a fairly brisk cellular reaction in the C.S.F. On no occasion, however, has there been any clinical sign of meningeal reaction, and serial examinations of the C.S.F. have shown that the only constant change is a rise in the protein content with excess of globulin and a minor alteration in the colloidal gold curve. These changes soon revert to normal, and may be regarded as of no clinical significance. On one occasion the cell content of the C.S.F. rose to 11 lymphocytes after the second injection, but the striking change lay in the protein elevation to 400 mg. in one case, this having reverted to levels of 60–120 mg. within the space of two to three weeks. These relatively minor changes in the C.S.F. have been rather surprising, but they indicate the relative blandness of phenol in glycerin when introduced into the theca.

Clinical Cases

We have now been able to observe the effect of treatment in 32 patients, some of whom received up to six separate injections, so that the actual number of intrathecal injections given is 75. From the diagnostic point of view the cases comprise the following:

Multiple sclerosis	21 cases
Parkinsonism	3 „
Syringomyelia	2 „
Hemiplegia of vascular origin	3 „
Spastic paraplegia—probably spinal type of disseminated sclerosis	2 „
Amyotrophic lateral sclerosis	1 case

From the functional point of view these cases could be reclassified in the following way. Six patients were mobile but had considerable spasticity in the lower limbs; the remainder were all chair- or bed-ridden. All but one were suffering from severe painful extensor or flexor spasms, the exception being one of the patients with syringomyelia whose leg was in a state of constant though painless extensor spasm.

Results of Treatment

It would be very gratifying to be able to record that this method of treatment has been an unqualified success, but unfortunately this is not the case. In general, however, the technique has proved of symptomatic value, and the following broad statements may be made about the results.

1. No mobile patient has been rendered completely immobile by the technique. In five cases mobility has been appreciably improved, with satisfactory reduction in the degree of spasticity and some improvement in function. In one of the mobile patients suffering from syringomyelia a severe degree of unilateral spasticity was converted to flaccidity of such degree that she was unable to walk for a period of two weeks, and now can walk only with great difficulty. In her case the total effect of function has been to her disadvantage, though from the academic point of view the spasticity has been completely abolished.

2. Rigidity of the lower limb due to Parkinsonism is significantly improved by phenolization, but tremor is unaffected.

3. It is the immobile patient suffering from painful flexor and/or extensor spasms who can most often be helped. The majority of the patients discussed here were suffering from multiple sclerosis and were bedridden. The main aim of treatment was to attempt to abolish painful spasms, and in every case this aim was achieved at least temporarily. In most cases the benefit has lasted for several months. It is thus possible to convert such patients from a painful life in bed to a chair-life of moderate comfort. Many of them were not able to sleep on account of the painful spasms and in particular they have derived great benefit from relief of this aspect of their problem. In two such cases—one of multiple sclerosis and one patient bed-ridden as a result of a vascular hemiplegia—return to walking was achieved after phenolization with the aid of orthopaedic manipulation of hamstring contractures and subsequent intensive physiotherapy. However, this conversion of an immobile patent to mobility is exceptionally rare. On the other hand, the abolition of the extreme spasticity may permit patients, still bed- or chair-ridden, to move and to be moved about in bed or in their chairs much more easily. The power which has been masked by the spasticity is unmasked by the process of phenolization, with obvious benefit. Almost universally the painful element of the spasm is removed or greatly diminished even if the motor factor is not improved.

4. As mentioned earlier, the major hazard concerns the disturbance of the urinary bladder and sphincter. In four of the cases treated, urinary control had already been lost before phenolization was carried out, and no change in sphincter status occurred. In four other cases the patients had already experienced some precipitancy and hesitancy of micturition, and in three of these retention developed after the first injection of the phenol. When this happened we immediately instituted tidal irrigation, and in two of the four cases the retention cleared within the space of three to four weeks. In the third case, after clearing the sphincter disorder has returned, and in the fourth case retention still persists after a period of seven weeks and seems likely to do so. Cystometrograms carried out in these cases indicate that the bladder is atonic. In this last case there is little doubt that the adverse effect upon the bladder was due to the fact that the phenol reached too low a level after injection. Maximum relaxation in this case was achieved

at the ankle, and after the first injection there was very little change in the degree of spasticity at the knee. This patient had acquired a pronounced scoliosis as a result of his neurological lesion, which has been developing over a period of 10 years, and it seems that, despite efforts to prevent the downward movement of the phenol solution, roots as low as S 1 were affected. Later injections were carried out on this patient at a higher space with greater elevation of the buttocks and successful relief of the extreme spasticity in the leg.

Duration of Benefit

It is not yet possible to be definite about the expected duration of the reduction in spasticity, for the effects vary greatly from patient to patient. It is now over three years, however, since an intrathecal injection was carried out in an elderly patient who had developed a spastic flexion paralysis of the left leg as a result of a cerebrovascular (thrombotic) accident. Phenolization was carried out by one of us (R. M. M.) in April, 1956, using 1 ml. of phenol 5% in glycerin at a level of L 2/3. The pain and flexor spasms ceased immediately, and by the aid of physiotherapy the leg was gradually brought into extension. This patient is still ambulant three years later. Another female patient suffering from multiple sclerosis, which resulted in very frequent painful flexor spasms and made sleep almost impossible for her, received two injections, each of 1 ml. of intrathecal 5% phenol, in November, 1957. For six months pain and spasm were completely abolished, but then the spasms began to recur, though, curiously enough, without any associated pain. Two further injections at L 2/3 were carried out in January, 1959, with success, and when last seen (September, 1959), she was still completely relieved, though of course quite immobile.

At the other end of the time scale we have one patient in whom flexor spasms, seemingly abolished by intrathecal injection, returned within one week of treatment though again the pain element had been removed. We feel that in this particular patient the pathological process (multiple sclerosis) is still active and that this may be responsible for the return of spasticity on each occasion. In the main, however, it seems that appreciable benefit can be expected for an average of at least six to 12 months, though further observation may cause us to modify this opinion. Two patients (each suffering from active multiple sclerosis) have died within three months of the treatment being carried out, though in neither case did it appear that the procedure had acelerated the underlying disorder, and in both cases severe pain and flexor spasms were relieved. We have concluded, however, that it is probably inadvisable to administer this form of treatment to patients in whom the demyelinating process appears to be active.

Summary

The technique of intrathecal injection of the solution of phenol in glycerin is described, and the results of its administration to 31 patients are discussed. The manœuvre is thought to be of circumscribed value in the relief of painful spasms in cases of spasticity. Careful positioning of the patient is required, and the possibility of resultant retention is emphasized. Care should be exercised in administering the treatment to patients who are still ambulant.

A number of the patients discussed in this paper were under the care of Dr. Fergus R. Ferguson and Dr. G. E. Smyth, to whom we are indebted for interest and advice. It is with pleasure and gratitude that we acknowledge a substantial grant from the Multiple Sclerosis Society in connexion with this work.

ADDENDUM.—Since this article was submitted for publication two others have appeared on this subject, both in the *Lancet*, December 19, 1959. The first, by P. W. Nathan, deals with the use of 20% phenol solution in cases of spastic paraplegia in flexion, and the second, by R. E. Kelly and P. C. Gautier-Smith, with problems very similar to those discussed in the article.

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BIOASSAY OF THEOPHYLLINE PREPARATIONS USING HUMAN SUBJECTS

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The two chief disadvantages ascribed to theophylline are well known ; it is poorly absorbed, probably because of low solubility, and it produces gastric irritation. To overcome these disadvantages, numerous theophylline salts and complexes have been introduced. In this investigation, using pure theophylline as a control, we have attempted to establish a hierarchy of clinical effectiveness among the various compounds by comparing the height and duration of blood levels which they produce in normal subjects and patients.

Method

Normal Subjects.—A group of 12 normal subjects, 21 to 35 years of age, selected at random, were used to study the blood levels of the preparations. Except for one subject (N. E. G.) all were males. At intervals of seven days, each subject received a single oral dose of each preparation listed in Table I in a dose equivalent to 400 mg. of theophylline.

Patients.—A group of 10 patients, 45 to 72 years of age, suffering from bronchial asthma, coronary artery disease, or primary hypertension each received a single

TABLE I.—*Preparations Used to Obtain Comparative Blood Levels in Normal Subjects*

Preparation	Theophylline Content (%)	Dosage Form
Aminophylline (theophylline ethylenediamine)	75–82	Capsule
Oxtriphylline (choline theophyllinate)	64·4	Coated tablet*
Theophylline	100	Capsule
Theophylline-choline	50	Coated tablet*
7-Hydroxyethyltheophylline	89	Capsule

* Commercial tablets were used.

dose of theophylline-choline* and their blood levels were compared with those of the normal subjects.

Both subjects and patients were in a 10- to 12-hour fasting state, and were told not to take barbiturates, coffee, tea, chocolates, or cola drinks during the testing periods, which occurred at seven-day intervals. Blood samples were drawn and heparinized before the administration of each drug for the "blank" and then at 15, 30, 60, 120, and 240 minutes afterwards.

Blood theophylline levels were determined by the double extraction method of Schack and Waxler (1949).

Results

Theophylline levels were measured in micrograms per millilitre of whole blood. As can be seen from Figs. 1 and 2 and Table II, theophylline rose to a peak of 4.5 ± 1.7 in 60 minutes and remained elevated for another 60 minutes. Aminophylline showed a peak of 4.2 ± 2.3 in 15 minutes and remained statistically constant for 240 minutes. Choline theophyllinate showed low initial levels that reached a peak of 5.5 ± 0.6 in 240 minutes. The 7-hydroxyethyltheophylline showed a level of 1.0 ± 0.5 in 15 minutes and remain statistically constant for 240 minutes.

Subject A.G.G. received a single dose of 1,200 mg. of choline theophyllinate, and a peak blood level concentration of 9.0 occurred in 120 minutes.

In an additional study on a subject, B.G., the single dose of pure theophylline produced a detectable blood level after 24 hours.

Discussion

The blood levels obtained on the normal subjects acting as their own controls revealed that aminophylline produced the highest levels in the first 15 minutes. Between 120 and 240 minutes no statistically significant difference was found in the theophylline blood levels when theophylline, aminophylline, or choline theophyllinate was administered. The low initial levels of choline theophyllinate and theophylline-choline are probably due to the tablet coating. Since there was no statistically significant difference in blood levels between the normal subjects and patients (Fig. 3), it may be assumed that theophylline-choline was absorbed equally well in both groups.

*These tablets are a simple mixture containing 100 mg. of theophylline (anhydrous), 0.05 mg. of reserpine alkaloid, and 209 mg. of choline bitartrate (equivalent to 100 mg. of choline), and supplied as "theracor" by Carroll Dunham Smith Pharmacal Co., New Brunswick, New Jersey.

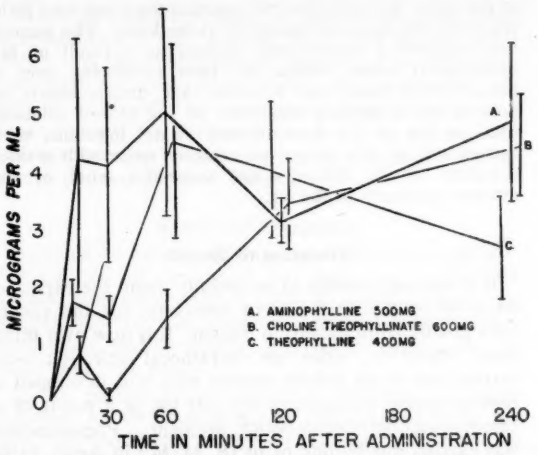

FIG. 1.—Blood theophylline levels after oral administration of a single dose of equivalent amounts of this drug to normal subjects.

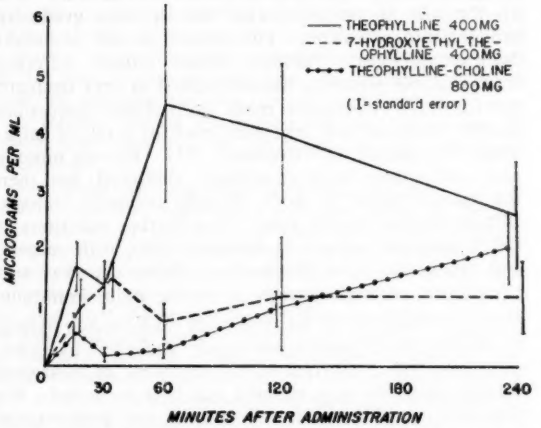

FIG. 2.—Blood theophylline levels after oral administration to normal subjects.

These findings confirm those of Waxler and Schack (1950) as well as those of Schluger, McGinn and Hennessy (1957), who also reported the rapid appearance of theophylline in blood after the ingestion of uncoated aminophylline tablets.

Though pure theophylline is less soluble in water at room temperature (1:120) than the other two prepara-

TABLE II.—*Whole-blood Levels (μg./ml.) Obtained in Normal Subjects*

Name	15 Minutes					30 Minutes					60 Minutes					120 Minutes					240 Minutes				
	A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	B	C	D	E
V.R.A.	13·3	2·0	1·2	0·0	1·0	10·0	1·1	4·1	0·0	1·0	12·0	1·0	4·4	0·0	1·0	3·1	4·1	3·5	0·0	1·0	8·0	9·0	4·6	0·0	1·0
P.B.B.	3·0	0·0	3·0	0·0	2·0	2·5	0·0	0·7	0·0	0·0	0·0	0·0	6·7	0·5	0·0	2·3	0·0	5·8	0·5	0·0	0·0	2·1	4·8	4·0	0·0
H.R.C.	—	0·0	1·7	0·0	—	—	0·0	2·5	0·0	—	—	0·1	2·9	0·1	—	—	3·4	3·1	0·0	—	—	2·0	8·9	1·1	—
R.R.F.	—	0·3	2·0	0·0	0·0	—	0·0	0·2	0·0	2·0	—	5·3	12·9	0·0	2·0	—	6·0	16·3	1·43	0·0	—	2·1	1·3	2·0	4·2
A.G.G.	0·0	0·0†	0·0	0·0	4·2	0·2	1·2†	0·0	0·0	8·0	3·5	7·0†	5·1	0·0	0·9‡	3·0	9·0†	0·5	0·0	8·0	2·4	7·3†	0·8	4·0	—
N.E.G.	0·0	0·0	2·7	1·9	0·0	5·5	0·0	0·5	0·0	0·0	3·0	0·0	0·0	0·0	0·0	4·0	3·0	0·0	0·0	0·3	3·2	3·1	0·0	0·0	3·3
R.L.G.	0·0	0·0	3·7	0·0	0·3	0·4	0·0	1·5	0·2	1·0	1·4	3·2	1·7	0·0	0·2	2·6	7·0	1·3	0·1	0·0	4·8	2·3	0·8	0·1	0·0
I.I.I.	—	0·0	—	0·0	—	—	0·0	—	0·0	—	—	0·1	—	0·8	—	—	2·2	—	0·0	—	—	4·2	—	0·0	—
G.G.K.	0·1	3·0	0·0	0·0	0·0	0·0	0·0	0·9	0·0	0·0	3·0	1·0	—	0·0	2·0	4·0	6·4	3·8	3·4	0·0	4·0	9·0	0·0	4·0	0·0
C.J.P.	13·0	0·0	1·2	5·0	0·2	10·0	0·0	2·2	2·0	0·3	12·1	0·0	2·6	2·0	0·1	3·0	0·0	2·2	2·0	0·1	11·3	2·0	2·0	1·3	0·0
B.J.S.	—	2·4	—	0·0	—	—	0·3	—	0·0	—	—	1·7	—	0·0	—	—	3·7	—	0·0	—	—	8·0	—	2·0	—
N.D.W.	—	1·0	—	0·0	—	—	0·0	—	0·0	—	—	3·0	—	0·0	—	—	1·0	—	0·0	—	—	5·0	—	0·0	—
Mean average	4·2	0·8	1·7	0·5	1·0	4·1	0·1	1·4	0·2	1·5	5·0	1·4	4·5	0·3	0·8	3·1	3·4	4·0	1·0	1·2	4·8	4·4	2·6	2·0	1·2
S.E. ..	2·3	0·5	0·4	0·4	0·5	1·7	0·1	0·4	0·1	0·3	1·8	0·5	1·7	0·1	0·3	0·4	0·8	1·2	0·3	1·0	1·4	0·9	0·9	0·6	0·0

† Dose of 1,200 mg. of choline theophyllinate (not included in statistical analysis). A=Aminophylline, 500 mg. B=Choline theophyllinate, 600 mg. C=Theophylline, 400 mg. D=Theophylline-choline, 800 mg. E=7-Hydroxyethyltheophylline, 500 mg.

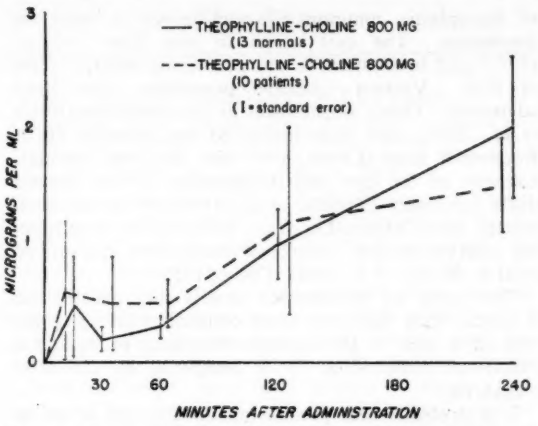

FIG. 3.—Comparative blood levels after oral administration of theophylline-choline to normal subjects and patients.

tions, it has been pointed out by Nelson (1957) that it is the solution rate rather than the solubility in a medium which determines blood levels. In order to determine whether there was any correlation between these findings and the clinical effectiveness of these various preparations, we used as a test subject a patient who had been under our continuous observation for the past three years.

Bioassay

A. H., a 69-year-old man, was under medical treatment for chronic bronchiectasis complicated by bronchial asthma. The number of asthmatic attacks he had experienced had been decreased by daily injections of 0.25 ml. of adrenaline 1:1,000 as the sole drug. Various oral theophylline preparations were administered to determine their effect on the number of injections required for the relief of his attacks as well as his vital capacity.

The drugs were administered by a modified double-blind technique. A plain gelatin capsule was used as the placebo for pure theophylline, aminophylline, and 7-hydroxyethyltheophylline. Because choline theophyllinate and the theophylline-choline preparation were in the form of yellow coated tablets, similar-appearing placebo tablets were used as controls for them.

TABLE III.—*Preparations and Dosages Used in Bioassay of Theophylline in Human Subject*

Preparation	Dosage Form	Initial Daily Dosage (mg.)	Maximum Daily Dosage (mg.)
Aminophylline	100-mg. plain tablet	200	1,200
Choline theophyllinate ..	200-mg. coated ,,	400	2,400
Theophylline	100-mg. capsule	200	1,600
Theophylline-choline ..	200-mg. coated tablet	400	1,600

TABLE IV.—*Results Obtained by Oral Administration of Various Theophylline Preparations*

Drug	Total Daily Dosage	Theophylline Equivalent (mg.)	Daily Doses of Adrenaline (0·25 ml., 1:1,000) Required	A.I.*	Vital Capacity (L.)
			Mean ± S.E.		
Placebo	—	—	5·2 1·2	100	1·7
Adrenaline	0·25 ml. (1:1,000)	—	— —	—	2·5
Aminophylline ..	800 mg.	640	3·0 1·0	58	2·1
,, ..	1,200 ,,	960	2·0 0·2	38	2·4
Choline theophyllinate	1,600 ,,	1,040	2·6 1·1	50	2·0
Theophylline	2,200 ,,	2,200	2·0 1·1	38	2·3
Theophylline-choline	2,400 ,,	1,200	2·3 1·0	44	2·1
Theophylline	1,600 ,,	1,600	1·7 1·7	33	2·0
Theophylline-choline	3,200 ,,	1,600	1·8 0·9	35	2·0

* See text.

During the test period the patient alternately received placebo for three-day periods and a theophylline preparation for three-day periods. Each preparation was given by the step-dosage methodology and each dosage level was administered for a three-day period. The preparations used and the dosage ranges are shown in Table III. The maximum daily dose was limited by the number of tablets or capsules which could be administered.

The results obtained are shown in Table IV. The various preparations are listed in ascending order of theophylline content, which ranged from 640 to 1,600 mg.

In order to amplify the changes produced in the daily adrenaline requirements, the following formulation was devised:

$$\text{adrenaline index (A.I.)} = 100 \times N_1/N_2,$$

where N_1 represents the number of adrenaline injections when the test theophylline preparation was administered orally and N_2 denotes the total number of adrenaline injections when no theophylline preparation was used.

In general, the A.I. quantitated the therapeutic effectiveness of various theophylline preparations in bronchial asthma, since there was a gradual reduction of the A.I. with increased theophylline dosage. This indicates that as the dosage of theophylline is increased the duration of action is prolonged, resulting in reduced requirement for adrenaline injections. On the other hand, the change in vital capacity did not vary in the same direction. The vital capacity increased by approximately 24% regardless of the dosage of theophylline administered and by 48% after the administration of adrenaline.

These data suggest that blood concentrations and clinical effectiveness of the various theophylline preparations depend on the dosage of pure theophylline present after the various agents undergo hydrolysis in the gastric juice. As a matter of fact, various workers (Truitt, McKusick, and Krantz, 1950; Turner-Warwick, 1957; Seppälä and Kärkelä, 1959) have shown that the minimum blood level of theophylline which is essential for diuresis or the relief of bronchospasm is 5 μg./ml.

In clinical practice, therefore, "the problem of reducing side-effects while retaining therapeutic effectiveness is virtually insoluble, for the active principle of all these xanthine derivatives is, in fact, theophylline" (*British Medical Journal*, 1957).

Summary

When single doses of four different theophylline preparations were administered to normal individuals, no statistically significant difference could be detected in blood concentrations from 120 to 240 minutes.

The adrenaline index revealed that the clinical effectiveness of various theophylline preparations depends on the absolute amount of theophylline present. Large doses produce an increase in duration of action rather than in intensity of action.

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Medical Memoranda

Pseudocholedochus Cyst

Choledochus cyst has been well described on many occasions, and Alonso-Lej *et al.* (1959) have gathered 419 cases from the world literature, analysing 92 of them. There is, however, no published account of pseudocholedochus cyst, though it is likely, in view of the variety of causes ascribed to choledochus cyst, that some of the cases reported may have been of this nature. It is necessary to make the distinction in view of the difference in treatment.

CASE REPORT

A baby, born on December 3, 1957, was admitted to hospital when 3 months old on account of refusal to take her feeds for the previous three weeks. The mother had noticed that the stools had been pale and offensive. Examination at this time showed no abnormal physical signs, but the stools were putty-coloured and contained soap plaques and casein. The feeds were acidified and the stools seemed to contain less fat. The abdomen began to increase in size, and the lower edge of an enlarged liver could be felt. Serum cholesterol was 200 mg./100 ml., and fasting blood-sugar was 81 mg./100 ml. It was thought that she might have glycogen-storage disease, and she was transferred to the Hospital for Sick Children, Great Ormond Street.

Examination on admission on March 21, 1958, showed a not seriously ill baby with a grossly enlarged abdomen, the girth being 22 in. (56 cm.). The enlargement was due to ascites, and paracentesis withdrew heavily bile-stained fluid.

On March 22 Mr. David Waterston opened the abdomen through an upper transverse incision. There was a small amount of free fluid in the peritoneal cavity, but what had been thought to be ascites proved to be an enormous cyst filling the lesser sac, displacing the stomach upwards and the transverse colon downwards. The cyst was incised and the fluid aspirated, 36 oz. (1,020 ml.) being collected. The boundaries of the cyst were those of the lesser sac. The liver, stomach, and remainder of the abdominal contents were normal. Immediately superior to the pylorus and first part of the duodenum was an area of fat necrosis. This was explored with a pair of divulsors which quickly entered a small cavity, from which pure bile welled up. This cavity connected with the common bile-duct, but it was not possible to establish the exact relationship. As much as possible of the anterior wall of the cyst was excised, and the abdomen was closed with a drain in the lesser sac and a second drain to the area of fat necrosis.

The baby made an uneventful convalescence from the operation. There was no drainage from the cyst, but 2 to 4 oz. (57 to 114 ml.) of bile was drained daily (via the second drain) for 12 days, when it ceased spontaneously. Six weeks after the operation she was discharged home fully recovered.

She has been seen subsequently as an out-patient, and continues to be free from any symptoms, and examination reveals nothing abnormal apart from a palpable spleen.

COMMENT

Choledochus cyst is a dilatation of the extrahepatic biliary tree (occurring typically in girls in their teens). The dilatation progresses slowly until a cystic mass forms in Rutherford Morison's pouch. The cystic dilatation most commonly affects the common bile-duct, and entering superiorly are the common hepatic duct, or the right and left hepatic ducts separately, and cystic duct, and from some part of the cyst a short segment of hypoplastic common bile-duct leaves to enter the duodenum. The cyst varies in size from 2–3 in. (5–7.5 cm.) in diameter to one containing nearly 5 litres of fluid. Various operative procedures have been advocated. Direct anastomosis to the duodenum (Keith *et al.*, 1957), and anastomosis to the jejunum via a Roux-en-Y loop (Grove, 1957) are the most popular. Excision of the cyst and implantation of the hepatic ducts separately (Shallow *et al.*, 1943) or the common hepatic duct (Alonso-Lej *et al.*, 1959) to the duodenum has been performed. Simple drainage of the cyst proved fatal in 20 out of 21 cases (Gross, 1953).

The cause of choledochus cyst is not certain, but it seems likely that it is some congenital defect in the wall of a part of the common bile-duct, producing a functional obstruction. It is compared by Gross to megaureter.

It is probable that pseudocholedochus cyst arises in a similar fashion to pseudocyst of the pancreas. This has been shown experimentally by Karlan *et al.* (1958) to arise when there is interference with the normal drainage of the pancreatic duct and fluid is poured into an enclosed space which remains in communication with the duct. In the case reported, bile had escaped through a defect in the common bile-duct into the lesser sac, where it had accumulated to form a cyst of great size. The cause of the defect was not known. McCredie (1957) described the cases of two children who had sustained severe injury resulting in rupture of the common bile-duct; in one it drained into the peritoneal cavity and required aspiration on four occasions, and in the other an external biliary fistula formed, which healed spontaneously. Tagart (1957) gives an account of a spontaneous rupture of a choledochus cyst.

In the case here reported there was no history of injury, nor was there any sign of a choledochus cyst. Treatment of this pseudocyst was by excision of as much of the wall as was possible, and simple drainage. Had this been a true choledochus cyst, such treatment would not have been effective.

I thank Professor A. A. Moncrieff, under whose care the baby was admitted, and Dr. David Waterston, who performed the operation, for their kind permission to publish this case.

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A new British Standard (B.S. 3233:1960) specifies requirements for pressure steam sterilizers of small size and with independent steam supply, used for the rapid sterilization of unwrapped instruments and utensils. Copies may be obtained from the British Standards Institution, Sales Branch, 2, Park Street, London, W.1. (Price 4s., postage extra to non-subscribers.)

Reviews

DR. LIVINGSTONE'S LETTERS

David Livingstone. Family Letters, 1841–1856. Volume I: 1841–1848; Volume II: 1849–1856. Edited with an introduction by I. Schapera. (Pp. Vol. I: 253; Vol. II: 320. 60s. the set.) London: Chatto and Windus. 1959.

These two volumes of the family letters of David Livingstone add to the already large collection of books about this remarkable man. One might be tempted to ask what more can be said about him and his work. However, it is in the reading of these very personal communications, a large number published for the first time, that one gets an even closer insight into the character of the man, always quite definite in his opinions as to how he should conduct his work, often intolerant of opposition, very critical of the actions of others, including his brother missionaries if they did not agree with him, outspoken to a degree, on occasion letting himself go in a manner which rarely occurs in his more formal journals, and at times almost neo-Shavian in his spelling of the English language. The true Scot comes out into the open in demonstrations of a pawky humour. The letters are those of a man dedicated to the service of God, who, though possibly slightly flattered that the outside world should confer honours on him, discounts these and takes no personal credit.

One is left with the indelible impression that Livingstone was first and foremost a missionary of the Gospel of Christ, secondly an explorer of the unknown. His qualifications as a doctor of medicine seem at times to supply merely additional skills which enable him to stand out as a pioneer of the two principal passions of his life: the glorification of God and the furtherance of the dignity of the British race.

The editor demonstrates not only a very comprehensive personal knowledge of Bechuanaland (where Livingstone worked) and its languages but also the capacity for taking infinite pains to ensure accuracy. One small criticism of the book might be that the maps could be better, more numerous, and more distinct in outline.

Read in conjunction with many works about Livingstone, these letters add greatly to their interest, as the many cross-references supply missing parts in the jigsaw puzzle of this wonderfully interesting life.

J. C. A. DOWSE.

HYPERTENSION

Hypertensive Disease. Diagnosis and Treatment. By Sibley W. Hoobler, M.D. (Pp. 353+x. 60s.) New York: Paul B. Hoeber, Inc. 1959.

Hypertension. The First Hahnemann Symposium on Hypertensive Disease. Edited by John H. Moyer, M.D. (Pp. 790 +xxii; illustrated. 98s.) Philadelphia, London: W. B. Saunders. 1959.

The increasing number of monographs on hypertension stems from the substantial advances which have been made in its treatment in the last decade. Effective drug reduction of blood-pressure was developed largely as a result of the perseverance and energetic advocacy of Smirk in New Zealand, and it is slightly disappointing that in these two American monographs there is only meagre acknowledgment of his pioneer efforts and important basic studies.

Hoobler's monograph is an excellent reference work for all clinicians interested in this subject. The book falls into three main sections: the first is on secondary hypertension susceptible to cure, the second deals with the treatment of primary or essential hypertension, and the third gives details of the various pharmacological agents available for control of the disorder. In each section the literature is well documented and illustrative case histories are used to promote appreciation of the author's practical clinical approach. The book is well balanced and can be highly recommended. It represents the experience and considered outlook of a clinical investigator with a high reputation in this field.

The second work, edited by Moyer, is a detailed report of original papers given at a symposium in Philadelphia, including recorded discussion by the ninety experts in attendance. Papers will be found here on every conceivable aspect of the subject from pathology through haemodynamics to pharmacology and surgery. Established ideas are fully discussed and presented with the addition of recent original observations, while other ideas such as the relationship of trace metals to hypertension will be new to most readers. The place of electrolytes and the possible relationship of disturbances of the suprarenal cortical hormones to hypertension are fully discussed. Every drug in use at the time of the symposium finds a place. The index is adequate and makes the research reports of considerable value for other investigators. Professor Moyer and the publishers are to be congratulated in producing a large and well-edited volume in record time. Such overlap and duplication as may occur is of interest in promoting free expression of varying points of view.

The trouble with new monographs on hypertension these days is that they are all out of date by the time they are published. Recent drugs, such as guanethidine and bretylium, which represent significant advances, are too new for inclusion in these volumes. Nevertheless each in its own particular way is a compendium which should be on the shelves of every medical-school library and of all investigators engaged in a study of this stubborn but slowly yielding problem.

J. MCMICHAEL.

GYNAECOMASTIA

Gynaecomastia. By Peter F. Hall, M.D.(Sydney), M.R.A.C.P., M.R.C.P. Foreword by P. M. F. Bishop, D.M., F.R.C.P. (Pp. 157; illustrated. £A.1 15s.) Sydney: Australasian Medical Publishing Co., Ltd. 1959.

In a foreword to this book Dr. P. M. F. Bishop points out that, so far as he is aware, it is the only monograph that has ever been written on the subject, and he believes that when the problem of gynaecomastia is finally solved Dr. Hall's book will be regarded as one of the major contributions to that solution. With this appraisal I am in entire agreement. From Chapter I, "Definition," onwards it is a model of thoroughness and conciseness, as well as a refresher course in a very fair slice of general clinical endocrinology.

From biopsy and operative studies Dr. Hall concludes that, whatever the cause of gynaecomastia, the histological condition is very constant and most closely resembles that of breast tissue stimulated by oestrogens. Increased oestrogenic stimulation, therefore, is regarded as the mediator of gynaecomastia, and for this view some rather convincing evidence is presented. However, there is of course much more to gynaecomastia than this: puberty, prepubertal testicular failure, testicular tumours, orchitis due to mumps, leprosy and other

causes, *x*-ray destruction of the germinal epithelium, Klinefelter's syndrome, traumatic spinal paraplegia, dystrophia myotonica, hyperthyroidism, male pseudohermaphroditism, adrenocortical tumours, cirrhosis, haemochromatosis, re-feeding after malnutrition, bronchogenic carcinoma, and pulmonary tuberculosis—all these and other causes are fully discussed. In treatment, where operation to remove the excessive breast tissue becomes necessary, the early use of the Jerome–Webster technique (in which the breast tissue is removed through a curved incision at the junction of the areola and the skin of the chest wall, thereby avoiding unsightly and embarrassing scars) is strongly urged.

Full documentation, a good index, and high-quality production contribute towards making this a thoroughly recommendable book.

G. I. M. SWYER.

ATHEROMA AND THE ARTERIAL WALL

Connective Tissue, Thrombosis, and Atherosclerosis. Proceedings of a Conference held at Princeton, New Jersey, May 12–14, 1958. Edited by Irvine H. Page. (Pp. 316+x; illustrated. $9.50.) New York, London: Academic Press. 1959.

The current interest in atherosclerosis has resulted in the publication of several monographs dealing with biochemical, dietary, hormonal, and pathological aspects of the problem. In this book, which contains the proceedings of a conference held in May, 1958, the part played by the arterial wall in the formation of atheroma is given full and detailed consideration. Until modern techniques allowed precise study of the structure and histochemistry of connective tissue, the dynamic properties of the arterial wall were neglected. Indeed, it is not long since that the arterial wall was blithely regarded by many as a passive elastic and muscular tube for the passage of blood, and even now thought is not often given to the contribution of connective-tissue metabolism within the arterial wall to the formation of atheroma. Whether atheroma results from the primary deposition of fat or of fibrin on the arterial intima, or whether it is initiated by constant haemodynamic trauma to the arterial wall, each of these processes leads to a series of metabolic changes which are the mechanism of repair by connective tissue.

Understanding of the composition and properties of arterial connective tissue is fundamental to our interpretation of the aetiology of atheroma, and in this admirable book recent advances in this field are presented by a distinguished group of experts. The physical and chemical properties of collagen and fibrous tissue (Drs. Moon, Schmitt, Jackson, Gross, Dougherty, and Lansing), the process of calcification in connective tissue (Dr. Glimcher), the origin and functions of fibroblasts (Dr. Boucek) and their relation to the acid mucopolysaccharides (Dr. Meyer) of ground-substance, are considered in detail. In addition, Professor Duguid reviews some of the connective-tissue reactions to the deposition of fibrin on the intima; Dr. Astrup, Dr. Sherry, and others give an account of the role of blood coagulation and fibrinolysis in the formation of atheroma; and Dr. Gitlin considers the relationship of immunochemistry to atherosclerosis.

This book, so well introduced and edited by Dr. Page, will be welcomed by many closely interested in the aetiology of atheroma. It fills a gap in the existing books on this subject and will, with its full bibliography, be consulted often.

M. F. OLIVER.

ORTHOPAEDICS

Clinical Orthopaedics. Editor-in-Chief: Anthony F. DePalma. No. 13. (Pp. 393+xi; illustrated. 60s.) Philadelphia, Montreal: J. B. Lippincott Company. 1959.

A brief biography of Sterling Bunnell is included in this volume largely devoted to the hand. It records his devotion to the study of hand surgery, which was recognized throughout the world, and emphasizes the credit due to him as a teacher.

There is so much to study in this book on the one subject that the chapters on knee, foot, elbow, and hip are overshadowed, though a valuable contribution to joint surgery is found in DePalma's writing on "the role of the disks of sternoclavicular and acromioclavicular joints."

The hand is considered from every aspect, so that there is detailed information on its anthropology, anatomy, and function, and on many aspects of the effects of trauma, diseases, and tumours, as well as on the intricacies of treatment. The basic facts are described and illustrated with great care and discrimination by specialists determined to teach surgeons—whether general, plastic, or orthopaedic—the importance of early recognition and treatment of all hand lesions. The subject is essentially a practical one, but the chapters nevertheless provide a contribution to theory. The dramatic description of repair after mutilation will be of great value in planning operative treatment, but equally well described are the more common conditions, such as stenosing tenosynovitis and trigger digits. Thumb contracture and stiffness of finger-joints are stated to be difficult problems and their restoration is described. Information on plastic surgery and acute trauma, followed by a chapter on infection of the hand, deserve attention. A report on 134 operations for Dupuytren's contracture at Boston is worthy of study, even if the reader is disappointed at finding so brief a description of an operative technique which leads to such a high percentage of successful results.

This volume contains the cumulative index of Nos. 7 to 12, and, with its high standard of production and printing, is in line with the previous volumes in this series.

ST. J. D. BUXTON.

PSYCHOPHARMACOLOGY

Psychopharmacology Frontiers. Second International Congress of Psychiatry. Proceedings of the Psychopharmacology Symposium. Edited by Nathan S. Kline, M.D. (Pp. 533+xxiii. 72s.) London: J. and A. Churchill, Ltd. 1959.

Psychopharmacology moves at such a pace that a congress held in September, 1957, covers only a fraction of the drugs used in psychoses to-day. Nevertheless, the papers read at the congress are not out of date, as the three drugs on which most of the reports are based, reserpine, chlorpromazine, and iproniazid, are still of undiminished importance to-day. There were nearly 100 participants, and the book starts by a few pages of photographs covering all but three of the participants—a very pleasant visual aid in these days of ever-increasing numbers of workers in even the most specialized fields.

About one half of the book is devoted to clinical observations and the therapeutic successes obtained with reserpine and chlorpromazine. Some very interesting speculations about the mode of action of these substances are contained in the second half and will stimulate thought about a problem which we are obviously too ignorant to solve satisfactorily at the present time. One

of the recurring thoughts is that the inhibition of conditioned avoidance responses, so clearly demonstrated on animals given those drugs, may be of fundamental therapeutic value. Another is the view that the Parkinsonism produced is not to be regarded as a side-effect but as a necessary condition of the clinical improvement.

MARTHE VOGT.

FOUR PSYCHOLOGICAL ESSAYS

Fear, Punishment, Anxiety, and the Wolfenden Report. By Charles Berg. (Pp. 126. 20s.) London: George Allen and Unwin, Ltd. 1959.

It was characteristic of the late Charles Berg that, throughout his long and successful career as a popular expositor of the scope and rationale of psychotherapy, he never had recourse to the weapons of polemic. In the most timely of the four papers that go to comprise this small book Dr. Berg showed that he was not unskilled in their use. In contrast to those reviewers who were radically opposed to the main recommendations of the Wolfenden Report, most critics of the report's arguments have been mild and almost apologetic. Dr. Berg metaphorically took off his coat and went for these arguments tooth and nail, holding in effect that a committee made up for the most part of members totally ignorant of the subject of homosexuality could not very well arrive at searching or sensible conclusions. His essay on punishment is also timely, particularly in view of the movement in some quarters of public opinion and of the press to support the reintroduction of flogging.

In the two short papers with which the book concludes Dr. Berg struggled with the problems of anxiety and fear. While his own theories on these subjects cannot be said to advance our knowledge very much, they may nevertheless be registered as brave tries.

EDWARD GLOVER.

THE MISSING LINK

Adventures with the Missing Link. By Raymond A. Dart with Dennis Craig. (Pp. 251+xv; illustrated. 25s.) London: Hamish Hamilton. 1959.

When in 1924 Professor Raymond Dart recognized the Australopithecus fossil find from Taungs for what it was—that of a creature midway between man and ape—a storm of controversy burst: there were occasions when the existence of the specimen was pointedly ignored, occasions when his interpretation was flatly rejected. Several recent popular books have implied that Dart was hurt by the treatment he received and as a result retired from further investigations. The appearance of *Adventures with the Missing Link*, in which he recounts for the first time his version of the affair, is therefore welcome.

But what a curious book it is, especially for an author of Dart's stature! Starting with the recognition of the Taungs find, the theme threads its way through Dart's earlier years, the controversy, Dart's views on some problems of less ancient African peoples, Broom's discoveries at Sterkfontein and Kromdraai, the siege of Makapansgat and the cultural and fossil finds at that site, and the cultural status of the Australopithecinae to which the major part of the text is devoted. The book consists of a mixture of autobiography and argument, narrative and anecdote, in which ideas are thrown together in a style which in places comes perilously near sheer journalism; and its appeal will therefore be mainly popular. In view of this it is unnecessary to enumerate the points of detail at which criticism could be levelled. What is important is that this is a most revealing book from which the reader learns a great deal about Dart and his ideas on the group of creatures whose existence he was the first to discover.

D. F. ROBERTS.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received.

Mechanical Design of Laboratory Apparatus. By H. J. J. Braddick, B.A., Ph.D. (Pp. 47; illustrated. 6s.) London: Chapman and Hall, Ltd. New York: Reinhold Publishing Corporation. For the Institute of Physics. 1960.

Vertebrate Dissection. By Warren F. Walker, jun., Ph.D. Second edition. (Pp. 340+xii; illustrated. 30s.) Philadelphia and London: W. B. Saunders Company. 1960.

An Interdisciplinary Approach to Accident Patterns in Children. By Irwin M. Marcus, Wilma Wilson, Irvin Kraft, Delmar Swander, Fred Southerland, and Edith Schulhofer. (Pp. 79. $2.50.) Lafayette, Indianna: Child Development Publications of the Society for Research in Child Development, Inc. 1960.

The Pharmaceutical Pocket Book. Seventeenth edition. Published by the direction of the Council of the Pharmaceutical Society of Great Britain. (Pp. 576+xii. 30s.) London: The Pharmaceutical Press. 1960.

The Principles and Practice of Medicine. A Textbook for Students and Doctors. By Sir Stanley Davidson, B.A.Cantab., M.D., F.R.C.P.Edin., F.R.C.P.Lond., M.D.Oslo, F.R.S.Edin., and Past and Present Members of the Staff of the Department of Medicine, University of Edinburgh, and Associated Clinical Units. Fifth edition. (Pp. 1,112+xi; illustrated. 35s.) Edinburgh and London: E. and S. Livingstone, Ltd. 1960.

Struktur und Stoffwechsel des Bindegewebes. II Symposion an der Medizinischen Universitäts-Klinik Munster (Westf.), October 16-17, 1949 Edited by Professor Dr. W. H. Hauss and Dr. H. Losse. (Pp. 184+viii; illustrated. DM. 37.) Stuttgart: Georg Thieme Verlag. 1960.

L'Attivita del Consorzio e la Endemia Tubercolare nella Provincia di Torino. By Giuseppe Grosso and Vincenzo Calderato. (Pp. 119; illustrated.) Turin: Consorzio Provinciale Antitubercolare. 1960.

Encyclopedia of Medical Syndromes. By Robert H. Durham, M.D., F.A.C.P. (Pp. 628+xiv. £5 10s.) New York: Paul B. Hoeber, Inc. London: Pitman Medical Publishing Co., Ltd. 1960.

Das Innere Lymphgefässsystem der Organe: Anatomie-Pathologie-Klinik. By Ferenc Renyi-Vamos, D.Sci.M. (Pp. 447; illustrated.) Budapest: Akademiai Kiado, Publishing House of Hungarian Academy of Sciences. 1960.

Praktische Endokrinologie. By Professor Dr. A. Jores and Professor Dr. H. Nowakowski. (Pp. 312+xii; illustrated. DM. 49.50.) Stuttgart: Georg Thieme Verlag. 1960.

Physiology of Prematurity. Transactions of the Fourth Conference, March 25-27, 1959, Princeton, N.J. Edited by Jonathan T. Lanman, M.D. (Pp. 187; illustrated. $4.50.) New York: Josiah Macy, Jr., Foundation. 1960.

Manual of Applied Nutrition. Fourth edition. Nutrition Department, Johns Hopkins Hospital, Baltimore, Maryland. (Pp. 134. 24s.) Baltimore: Johns Hopkins Press. London: Oxford University Press. 1960.

Manual of Hospital Planning Procedures. (Pp. 72+viii. $1.50.) Chicago: American Hospital Association. 1960.

Ensuring Medical Care for the Aged. By Mortimer Spiegelman, F.S.A. (Pp. 280+xxvi. $5.75.) Homewood, Illinois: Richard D. Irwin, Inc. for the Pension Research Council, University of Pennsylvania. 1960.

Roentgenologic Diagnosis in Ophthalmology. By Edward Hartmann, M.D., and Evelyn Gilles, M.D. Translated by George Z. Carter, M.D. Edited by Conrad Berens, M.D., F.A.C.S. (Pp. 375+ix; illustrated. £6.) Philadelphia and Montreal: J. B. Lippincott Company. London: Pitman Medical Publishing Co., Ltd. 1960.

Clinical Orthopaedics. No. 15. Editor-in-Chief: Anthony F. DePalma. (Pp. 217+xii; illustrated. 60s. single copies; 48s. subscribers.) Philadelphia and Montreal: J. B. Lippincott Company. London: Pitman Medical Publishing Co., Ltd. 1960.

BRITISH MEDICAL JOURNAL
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THE TORQUAY MEETING

Torquay put on its best dress for this year's Annual Meeting. With one or two minor interruptions the sun shone clear and strong on inhabitants and visitors alike. The great day for all was when the Duke of Edinburgh arrived by helicopter on Torre Abbey Meadow, briskly strode into the Town Hall, took the chair at the Annual General Meeting, went round the scientific and pharmaceutical exhibitions at a rattling pace, presided at the presidential luncheon, inducted Sir Arthur Porritt as his successor to the presidency of the British Medical Association, and then flew his helicopter back to London to fulfil yet another public engagement. It was a red-letter day for the B.M.A., and our Royal immediate past-President must forgive us if for a moment we bask in the reflection of his urbanity, wit, and charm of manner; and no one could fail to be impressed by his quick perception of what was pertinent in the displays at the scientific exhibition, and the lively interest he displayed when listening to Sir Arthur Porritt's presidential address in the covered tennis court of the Palace Hotel. For one brief but glorious June day Prince Philip became what our American colleagues call a shirt-sleeves President.

If Torquay cannot provide the setting for pomp and pageantry of a university town or a cathedral city, it can give much else—blue seas, sheltered and sunny coves, handsome hinterland of moor, and warm friendliness of Devonshire people. Friendliness was the keynote of the meeting. Geniality even shone through the carefully contrived colonic jokes that spattered the speeches of those representatives who were rightly in earnest about cleaning up Britain's beaches. The civic authorities, from the Mayor and Town Clerk of Torquay downwards, put their buildings and services and ready smiles at the disposal of the 1,348 medical men and women who registered their attendance at the 128th Annual Meeting of the British Medical Association. Any car that carried the B.M.A. label seemed to escape the notice of the constabulary even when it stood all day in a place which an L-driver would have learnt to avoid. And, of course, the attitude of the town was what one might call a feed-back from our hosts, the South-Western Branch and the Torquay Division, under the genial guidance of Dr. S. Noy Scott and Dr. R. M. S. McConaghey, who with their wives were at all places at all times, seemingly unwearied in well-doing. All this was a fitting environment for our new President, Sir Arthur Porritt, who with Lady Porritt graced private and public occasion with a direct and warm friendliness that endeared them to the many who had this opportunity of getting to know them.

In the elaborate ritual of an Annual Meeting the medical and allied sciences have pride of place once the presidential address (published in last week's *Journal*) has been delivered. The attendance was good at the 20 scientific sections, beginning with anaesthetics and ending with surgery: the first meeting in the Electric Hall and the last in the Gas Showroom. These were backed up by symposia, panel discussions, a general session, and a debate in which 43 people were for and 44 against the subject "that dissemination of medical knowledge by means of television, radio, and the press does more harm than good to the health of the population." There were medical films on show. Messrs. Smith, Kline, and French once again justified their claim to help in educating the medical profession by sponsoring and producing programmes of closed-circuit colour television—this time from the Torbay Hospital to the Town Hall. The Scientific Exhibition had perforce to be held in slightly cramped quarters, but everyone from the Duke of Edinburgh downwards found it highly interesting. The technique of exhibiting improves each year, and the greater use of standard panels has made exhibitors concentrate on economy and simplicity of display. It is interesting to note that the judges awarded the prize for the best scientific exhibit to the Research Department of I.C.I. Pharmaceuticals for their investigation of the toxicity of a drug. And the positive achievements of research in the industry were well displayed in the Annual Exhibition of Pharmaceutical Products, etc., in the marquee in Upton Park.

Whatever may be the natural advantages of the place of an Annual Meeting, and however eminent may be the visitors to it, its general success is determined first and foremost by the men and women on the spot. Dr. S. Noy Scott and Dr. R. M. S. McConaghey, untiring themselves, were backed up by an equally tireless team. Dr. J. Macpherson as Chairman of the Local Executive Committee had as his able lieutenants Dr. A. Robinson Thomas as general secretary (with a special responsibility for good food and wine) and Dr. R. L. Midgley, who as

science secretary carried out a difficult task to a successful conclusion. Torquay has an awkward topography, but the skill of Dr. J. F. Burdon, in charge of transport, made it possible for those with a poor bump of locality to get to the places they wanted to get to. Dr. Agnes Kennie, who with a handful of colleagues had made a new banner to hang in the Great Hall at B.M.A. House, also saw to it that the ladies enjoyed every minute of their stay. Throughout the meeting members of the Junior Leaders' Regiment, Royal Signals, gave invaluable help as stewards, and this journal in particular received the most willing co-operation of the Torquay Times and Devonshire Press, Ltd. To everyone who made the Annual Meeting such a success the Association is indeed deeply indebted.

HORMONE TREATMENT OF METASTATIC BREAST CANCER

About twelve years ago the Therapeutic Trials Committee of the American Medical Association sponsored a rigidly controlled trial of the treatment of metastatic breast cancer by oestrogens and androgens. Over a period of 10 years 60 observers have submitted detailed observations on 1,983 patients, and the final analysis has recently been published.[1] It is an important and impressive document.

The stringent conditions for acceptance of case records were strictly enforced. Every case accepted was histologically confirmed as metastatic breast cancer untreatable by surgery or irradiation, and in no instance was the trial confused by the operation of any form of therapy such as irradiation, endocrine ablation, or the administration of a hormone of the opposite group during, and for six months before, each trial period. It is not surprising that of the 1,983 case records submitted, no fewer than 1,039 (52%) were rejected. The analysis of the remaining 944 cases permitted a valid comparison of the relative effectiveness of the two groups of hormones. It also revealed certain basic characteristics of the disease which will materially increase our knowledge of its complex life history.

Of the 580 women given androgens, tumour regression was induced in 21.4%. Among the 364 oestrogen-treated patients it was 36.8%. When the patients were compared in groups of the same post-menopausal age, there was a higher frequency of response to oestrogen at every decade. In both groups it was clear that the older the patient when hormone therapy started, the more likely was tumour regression to occur. In androgen-treated women the chance was less than 1 in 20 that this relationship was coincidental. On the other hand, in oestrogen-treated patients the correlation was much stronger, the chance that it was coincidental being less than 1 in 2,000.

The commendably high follow-up rate to the time of death (89.4%) clearly revealed that women whose disease temporarily regressed under hormone treatment had a significantly longer duration of life after starting treatment than those whose disease was not responsive. Of 427 women given androgen, the average duration of life of those who did not respond was 9.7 ± 8.4 months; for those who responded it was 19.1 ± 12.2 months, and the chance was less than 1 in 100 that the difference was coincidental. Of 243 women given oestrogens, the non-responders lived for 10.4 ± 10.8 months, while the responders survived for 27.3 ± 18.2 months; the difference was of greater significance for women given oestrogens than for those given androgens, the chance being less than 1 in 1,000 that it was coincidental.

The significant correlation between the occurrence of an induced regression of growth and the increase in life span which follows it proved to be the most constant effect of hormone therapy, and gave a clear indication that an artificially induced regression of growth profoundly alters the natural history of the disease.

There was no significant difference between oestrogens and androgens in their capacity to control skeletal or visceral metastases, but secondary growths in lymph nodes, skin nodules, and mammary tissue regressed more often in oestrogen responders (40.70%) than in androgen responders (18.2%). Seven pre-menopausal women were given oestrogens against the advice of the Committee, and without exception this was followed by *acceleration of growth*. The report has made a strong case for oestrogen therapy as the first choice in the hormonal treatment of breast cancer in post-menopausal women and advises that oestrogens should be used in preference to androgens after the fourth post-menopausal year.

The time elapsing between recognizing and treating a primary mammary cancer and the first clinical recognition of its blood-borne metastases varies from a few months to many years. A fruitful analysis of this interval, referred to in the report as the "*free interval*," was made by pooling 549 hormone-treated patients and dividing them into three groups. In the first (termed B1) both the primary and its

[1] *J. Amer. med. Ass.*, 1960, **172**, 1271.
[2] Hadfield, G. J., and Holt, J. A. G., *Brit. med. J.*, 1956, **2**, 972.
[3] —— *Ann. roy. Coll. Surg. Engl.*, 1959, **25**, 1.

metastases were recognized and treated before the menopause. In the second (B2) the primary was recognized and treated before the menopause, while its secondaries became activated after the menopause. In the third (B3) both primary and metastases were recognized after the menopause. The following table shows the average free interval for each group.

Group	Recognition of		No. of Patients		Free Interval	
	Primary	Metastases	Total	%	Years	Months
B1	Pre-meno.	Pre-meno.	124	22·6	2	7·36
B2	,,	Post-meno.	48	8·7	7	3·1
B3	Post-meno.	,,	377	68·7	3	3·2

It is clear that in 8.7% of 549 cases of breast cancer an inordinately long, clinically silent period averaging 7¼ years is associated with the interposition of the menopause between the clinical recognition of the tumour and the activation of its distant metastases. The characterization of this group is described in the report as "unique and hitherto unrecognized." This is a mistake, for E. F. Scowen described this association in his Langdon-Brown lecture (unpublished) to the Royal College of Physicians in 1955 and expressed the view that the menopausal state was one of the main factors in the induction of a naturally occurring regression of tumour growth in breast cancer. In 1956 G. J. Hadfield and J. A. G. Holt[2] reported 19 cases in this journal, and Hadfield[3] published a further analysis in 1959. There is no doubt, however, that at no time before the publication of this report has the profound influence of the menopause on the natural history of pre-menopausal breast cancer been subjected to so close a statistical study based on so impressive a number of carefully scrutinized case records. This laborious ten-year experiment has established a series of reliable baselines for future research. One of its major achievements is the successful isolation of the remarkable group of women who almost succeed in arresting the growth of their own metastases. It may be profitable to investigate the endocrinological status of this group of patients.

INTRA-ARTICULAR STEROIDS

In 1951 J. L. Hollander and his colleagues[1] reported on the effects of the intra-articular injection of cortisone and hydrocortisone. They found hydrocortisone to be much the more effective in alleviating local signs and symptoms. Seven hundred injections into the joints of 129 patients produced no untoward effects. The duration of improvement after the injection of 25 mg. into one or more joints of patients with rheumatoid arthritis varied from a few days to several weeks. Injections could be repeated without loss of benefit. The results in osteoarthritis were said to be even more satisfactory, remissions in some patients lasting several months. In a second report in 1953 Hollander[2] reviewed his own experience, based on 7,352 injections into synovial cavities. His series included 249 patients with rheumatoid arthritis, in whom worthwhile effects were attained in all but 6%. The average duration of relief was eight days and the highest dose injected into a single joint was 37.5 mg. hydrocortisone acetate. Adverse reactions occurred in 2.3%, the commonest being an exacerbation of symptoms lasting from 2 to 72 hours. Staphylococcal infection occurred in only one case. In another, deterioration followed treatment of what proved to be a tuberculous infection. Hollander concluded that the intrasynovial injection of hydrocortisone was a safe and useful palliative procedure in the local treatment of arthritis. These conclusions have received support from many workers throughout the world.

Only recently has the suggestion been made that this form of treatment may not be free from risk. In a controlled trial designed to compare the respective value of hydrocortisone acetate and hydrocortisone tertiary butyl acetate, G. N. Chandler and V. Wright[3] noted radiological deterioration in 13 out of 25 knee-joints treated, in spite of symptomatic improvement in the majority of cases. These authors believe that the main cause of radiological progression was the encouragement of a damaging level of physical activity by interference with a local protective mechanism normally associated with inflammation. The same group of workers[4] subsequently reported a further case in which gross destruction of the femoral head and acetabular roof occurred in a patient with osteoarthritis of the hip who had received 18 monthly injections of 50 mg. of hydrocortisone acetate into the affected joint. D. R. Sweetnam, R. M. Mason, and R. O. Murray[5] have described four cases in which rapid destruction of the femoral head occurred during the administration of steroids. In two instances steroids were given by mouth only. The authors believe that this condition is a steroid-

[1] Hollander, J. L., Brown, E. M., Jr., Jessar, R. A., and Brown, C. Y., *J. Amer. med. Ass.*, 1951, **147**, 1629.
[2] —— *J. Bone Jt Surg.*, 1953, **35A**, 983.
[3] Chandler, G. N., and Wright, V., *Lancet*, 1958, **2**, 661.
[4] —— Jones, D. T., Wright, V., and Hartfall, S. J., *Brit. med. J.*, 1959, **1**, 952.
[5] Sweetnam, D. R., Mason, R. M., and Murray, R. O., ibid., 1960, **1**, 1392.
[6] Norcross, B. M., *J. Amer. med. Ass.*, 1958, **167**, 839.
[7] Cardoe, M., *Proc. roy. Soc. Med.*, 1959, **52**, 1109.
[8] Zuckner, J., Machek, O., and Ahern, A. M., *Ann. rheum. Dis.*, 1956, **15**, 258.
[9] Kellgren, J. H., Ball, J., Fairbrother, R. W., and Barnes, K. L., *Brit. med. J.*, 1958, **1**, 1193.

induced arthropathy, brought about by diminution of pain, osteoporosis, and trabecular stress fractures. An accurate assessment of the risk of inducing further damage in arthritic joints by local steroids can be derived only from a trial in which radiological progression in treated and untreated joints is compared over an adequate period of time, but these reports suggest a need for caution.

B. M. Norcross[6] has claimed that large doses of hydrocortisone acetate (150–300 mg.) in a single injection gave very satisfactory results in the treatment of the knee-joints in rheumatoid arthritis. Doses of this order produced systemic as well as local effects, with improvement of untreated joints. M. Cardoe,[7] using a concentrated preparation of prednisolone trimethylacetate, injected 200 mg. into the knee-joints in cases of rheumatoid arthritis, and found the duration of improvement to be almost three times as long (5.7 weeks) as that after the injection of hydrocortisone acetate (2 weeks). No comment is made in either report of radiological changes in the treated joints. The use of such high doses might increase the risk of further local damage by more prolonged suppression of symptoms.

It would be most unfortunate if a method of treatment which has proved of value when used with discretion should fall into disrepute. There is obviously a danger that brilliant immediate results may encourage the indiscriminate use of large doses at too frequent intervals, with subsequent "crumbling" of the treated joints, particularly of the hip and knee. It would appear wise to limit the amount of steroid in a single injection to 40–50 mg. of hydrocortisone acetate in the case of weight-bearing joints. There is little evidence that the newer steroids are more effective when given in equivalent doses.[8] Repeated injections into a single joint at short intervals should be avoided in ambulatory cases. Patients should also be specifically warned against excessive use of the affected joints during the period of relief, but non-weight-bearing exercises to maintain stability should not be abandoned. Regular radiological examination would seem essential if repeated injections are considered necessary. This precaution may be even more important in patients already taking steroids by mouth. J. H. Kellgren and his colleagues[9] have indicated that suppurative arthritis may arise as a complication of severe rheumatoid arthritis. Any suspicion of infection is an absolute contraindication to the injection of steroids, and strict aseptic precautions should be maintained when injections are given. This is not a procedure for casual use in a busy surgery.

GENETIC RECOMBINATION IN BACTERIA AND VIRUSES

Genetic recombination was discovered in *Escherichia coli* by J. Lederberg and E. L. Tatum[1] in 1947. It had been found that, just as with fungi, treatment of bacterial cells with mutagenic agents gave rise to mutant strains which had specific biochemical deficiencies. Two strains having different growth requirements, obtained in this way, were mixed together and cultured in a rich medium containing all the substances necessary for the growth of either strain. Cells from this culture were then plated on a minimal medium containing only the growth requirements of normal bacteria. It was found that about one cell in every million could grow on the minimal medium, whereas there were none like this when the experiment was repeated using either parent strain alone. The implication of this was that, during the growth of the mixed culture, some process of exchange occasionally took place between the hereditary material of the two strains. Since the parental strains carried different biochemical deficiencies, their mutations involved different genes, and hence certain of the recombinants would carry none of the mutant factors and thus show no biochemical deficiency.

This selective technique for obtaining recombinant progeny, by mixing nutritionally deficient strains and ultimately plating on minimal medium, has formed the basis of a large part of the subsequent work on the genetics of bacteria and, in modified form, of bacterial viruses also. It is convenient to consider the mechanism of genetic recombination in bacteria in two stages: first, the transfer of hereditary material from one cell to another, and, secondly, its behaviour on arrival in the acceptor cell.

Three different mechanisms are known in bacteria by which genetic material is transferred from cell to cell. All three entail the one-way transfer of only part of the hereditary material, and hence differ fundamentally from the transfer of intact haploid nuclei characteristic of higher forms of life.

The transfer mechanism in *Escherichia coli* underlying Lederberg and Tatum's discovery of recombination has been found by E. L. Wollman and colleagues[2] to entail conjugation between cells of donor and acceptor strains. On mixing the two strains, contact between cells of each kind is thought to be determined by chance collision, but is followed by specific attachment. Conjugating cells can be observed under the microscope, and stereoscopic electron photomicrographs have been

[1] Lederberg, J., and Tatum, E. L., *Cold Spr. Harb. Symp. quant. Biol.* 1946 (1947), **11**, 113.
[2] Wollman, E. L., Jacob, F., and Hayes, W., ibid., 1956 (1957), **21**, 141.
[3] Griffith, F., *J. Hyg.* (*Lond.*), 1928, **27**, 113.
[4] Avery, O. T., MacLeod, C. M., and McCarty, M., *J. exp. Med.*, 1944, **79**, 137.
[5] Lederberg, J., Lederberg, E. M., Zinder, N. D., and Lively, E. R., *Cold Spr. Harb. Symp. quant. Biol.*, 1951 (1952), **16**, 413.
[6] Hotchkiss, R. D., *J. cell. comp. Physiol.*, 1955, **45**, Suppl. 2, 1.
[7] Lederberg, J., ibid., 1955, **45**, Suppl. 2, 75.
[8] Meselson, M., and Stahl, F. W., *Cold Spr. Harb. Symp. quant. Biol.*, 1958 (1959), **23**, 9.
[9] Watson, J. D., and Crick, F. H. C., *Nature* (*Lond.*), 1953, **171**, 964.
[10] Levinthal, C., *Genetics*, 1954, **39**, 169.
[11] Burnet, F. M., *Cold Spr. Harb. Symp. quant. Biol.*, 1958 (1959), **23**, 1.

prepared. By violent agitation of the culture at different times after mixing, Wollman and colleagues have made the remarkable discovery that genes are transferred from donor to acceptor cell in a definite time sequence, and furthermore this sequence corresponds with the sequence of the genes in the "chromosome" as determined from recombination frequencies in experiments of the "Lederberg and Tatum" type. Thus with a particular donor strain at 37° C. the gene for threonine synthesis enters acceptor cells eight minutes after mixing the cultures, the gene for leucine synthesis half a minute later, followed by that for sodium-azide resistance after a further half-minute, and so on. Spontaneous breakages occur frequently, so that even without agitation genes late in the sequence are usually not carried over, and at most only about half the hereditary material of the donor cell is transferred. However, in other donor strains the transfer of genes to the acceptor strain starts at different points in the "chromosome," or occurs in reverse sequence, so that collectively all the genes can be transferred, even if in no individual case is more than half transported.

A second method of transfer is genetic transformation, discovered in the pneumococcus by F. Griffith.[3] Later, O. T. Avery and colleagues[4] showed that the "transforming principle" was composed of deoxyribonucleic acid (D.N.A.). Genetic transformation is now also known in the meningococcus and in *Haemophilus influenzae*. If these bacteria are grown in a culture medium and then removed, and another strain of the same bacterium added to the medium, the latter strain is found to acquire characters of the former. There is no possibility of contact between cells of the two strains, and it appears that, after removal of the cells of the first strain, fragments of their hereditary material persist in the culture medium and some become absorbed into cells of the second strain. Griffith's original discovery of transformation referred to capsule characters, but it is now known that any inherited character, such as drug resistance or antigenic properties, can be transferred in this way.

A third method of transfer, genetic transduction, was discovered by Lederberg and colleagues[5] in *Salmonella typhi-murium*. Bacterial viruses can exist in a dormant form as prophage, when they occupy a specific locus on the bacterial "chromosome." When prophage becomes active, the phage particles liberated may carry some of the bacterial D.N.A. with them to another cell. In *Escherichia coli* only genes in the immediate neighbourhood of the prophage locus are carried over, though in *Salmonella* any gene may be transferred in this way.

Though the methods of gene transfer in bacteria are diverse, the behaviour of the "chromosome" fragments on arrival in the acceptor cell appears to be uniform. The genes transferred may function immediately in the acceptor cell. Thus, R. D. Hotchkiss[6] reports that addition of D.N.A. from a streptomycin-resistant strain of pneumococcus to a streptomycin-sensitive strain causes some of the cells to become resistant within a few minutes. It does not follow, however, that the progeny of such cells will necessarily inherit the resistance. Similarly, failure to inherit a phage-transferred character is of frequent occurrence, causing "abortive transduction." Indeed, only a small proportion of the genes transferred by whatever means become incorporated into the acceptor's "chromosome." It appears as if the transferred D.N.A. cannot be replicated as an isolated "chromosome" fragment, but only after it has paired up with the homologous part of the acceptor's "chromosome." It has been suggested[7] that new "chromosomes" are assembled progressively, the process starting from one end and the old "chromosome" being used as a template, and that, where homologous "chromosomes" are paired, a process of "switch-synthesis" or "copy-choice" may occur—that is, first one "chromosome" and then the other being used as a template. On this hypothesis, failure of a transferred gene to be inherited may be due to lack of pairing, or to copy-choice happening to favour the acceptor's allele.

However, a dilemma is presented by recent evidence about the mechanism of replication of D.N.A. M. Meselson and F. W. Stahl[8] used a strain of *E. coli* in which heavy nitrogen (^{15}N) had been incorporated in its D.N.A., and allowed the bacteria to multiply in a medium containing ordinary nitrogen (^{14}N). After each cell division, the distribution of ^{14}N and ^{15}N atoms in the D.N.A. was determined. It appears that the D.N.A. replicates by the method proposed by J. D. Watson and F. H. C. Crick[9]—that is, that the molecule splits longitudinally and a new complementary half is assembled alongside each old half. This method of replication is in conflict with the principle of copy-choice, which requires the new chromosomes to be composed wholly of new material, some parts like one parent chromosome and some like the other. To account for genetic recombination in bacteria, it may therefore be necessary to postulate breakage of homologous parts of chromosomes at corresponding points, followed by rejoining in new ways.

The viruses have several features in common with the bacteria. If two strains of a bacteriophage (a virus that infects bacteria) differing in two or more of their genes have discharged their D.N.A. into one bacterial cell, homologous parts of the D.N.A. may pair up. When replication occurs, opportunity for genetic recombination arises; it seems as if the replica may be copied partly from one parent and partly from the other. When phage multiplies, successive replicas are formed before maturation of the daughter phage particles and lysis of the host cell. Before each replication further recombination may take place. C. Levinthal[10] has shown that recombinants do not arise until the second replication after pairing. Sir Macfarlane Burnet[11] describes recombination between different strains of influenza virus, and suggests that the mechanism is probably similar to that of bacterial viruses. The suggestion that the periodic influenza pandemics, such as Asian 'flu in 1957, are the result of recombination between other strains seems plausible.

THE EYE OF THE PREMATURE BABY

In 1955 M. C. Fletcher and S. Brandon[1] and H. L. Birge[2] in the United States drew attention to the occurrence of high myopia in premature infants, and considered this to be a complication of retrolental fibroplasia, or of oxygen therapy. I. D. R. Gregory,[3] reporting on 18 cases in Great Britain in 1957, held very much the same views, but G. Wagner,[4] in a study in the same year in Germany, could not find any association between myopia and the administration of oxygen, for in 104 premature infants there were 10 myopes (4 with refractions over 10 D) who had not had any oxygen. In all, he observed 28 myopes in his series, of whom 7 had myopia from −0.75 to −3.0 D, and 8 myopia between −3.25 D and −6.0 D; 7 children had myopia from −6.5 D to −15.0 D, and 6 had myopia of 16 D, or more. The incidence of myopia among premature infants is therefore considerable, and is unrelated to retrolental fibroplasia. Furthermore, Wagner found that the incidence of abnormally high degrees of hypermetropia was also considerable, and he held that the more the refraction differed from emmetropia the lower had been the birth weight. The assumption that myopia in prematures is of necessity axial in character has not been proved; there is in fact no information on the optical components of the refractive errors in such children, and little is known of the course of these errors during growth. The view that high refractive errors in the premature baby represent a persistence of the foetal state requires both elucidation and confirmation.

Persistent pupillary membrane is a further aspect of prematurity. B. Gans[5] has emphasized the persistence of this network during the first few days of life. R. Schmöger[6] had previously noted that the frequency of persistent pulmonary membrane varies directly with the degree of prematurity. Thus in 18 infants with a birth weight of up to 1,000 g. (2.2 lb.), 17 examined on their day of birth showed persistent pupillary membrane; the incidence of such membrane dropped to 86.5% in 37 infants with a birth weight of 1,001 to 1,500 g. (2.2–3.3 lb.), to 74.5% in 51 infants with a birth weight of 1,501 to 2,000 g. (3.3–4.4 lb.), and to 40% in 20 infants with a birth weight of 2,001 to 2,500 g. (4.4–5.5 lb.). Slit-lamp examination shows minimal remains of such membranes as a not infrequent occurrence in adults, and the fact that the pupillary membrane is a normal feature in the embryonic eye readily explains its prevalence in the premature infant, and its ready tendency to disappear after birth. Persistence of the pupillary membrane may therefore be taken as an almost constant feature of the premature infant, but only in the first few days of life. It would be interesting to establish the validity of the belief that persistent hyaloid vessels also tend to occur frequently in premature babies.

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[2] Birge, H. L., *Trans. Amer. ophthal. Soc.*, 1955, **53**, 219.
[3] Gregory, I. D. R., *Brit. J. Ophthal.*, 1957, **41**, 321.
[4] Wagner, G., *Klin. Mbl. Augenheilk.*, 1957, **131**, 326.
[5] Gans, B., *Arch. Dis. Childh.*, 1959, **34**, 292.
[6] Schmoger, R., *Kinderärztl. Prax.*, 1955, **23**, 433.

DIURETICS AND GOUT

So far the only serious disadvantage of chlorothiazide and its derivatives has been the tendency to produce potassium deficiency. Recently, however, another side-effect has been recognized, which, though fortunately uncommon, is of great interest. This is the ability of these compounds, and especially hydrochlorothiazide, to cause acute attacks of gout in predisposed individuals.[1,2] It is well known that gout can be precipitated by a number of apparently unrelated factors, among them infections, operations, emotional stress, and prolonged bed rest. Similarly a variety of drugs which have little in common have also been implicated; these include penicillin, vitamin B_{12}, insulin, ergotamine, pyrazinamide, and steroids. Such a lack of specificity makes it difficult to visualize a common mechanism underlying the attack of gout. With diuretics, however, it may be possible to define at least part of the sequence of events.

Some years ago N. L. Price[3] described five patients who had developed gout during the course of a satisfactory diuretic response to mersalyl. A similar pattern is apparent with chlorothiazide—a gouty predisposition, a good diuresis, and prolonged use of the drug. There is no evidence that diuretics affect urate metabolism, and it seems more likely that alterations in electrolyte balance interfere with excretion of uric acid. This is borne out by the fact that when the concentration of uric acid in the serum has been measured it is almost invariably raised in patients taking thiazide diuretics for long periods.[4–6] Nevertheless the relation of hyperuricaemia to acute gout is by no means constant, and accumulation of urates in the body does not necessarily account for the precipitation of an acute attack. It would be of interest to know whether hyperuricaemia due to chlorothiazide has any adverse effect on the patient without a gouty diathesis, and a detailed study of the way in which the body deals with uric acid in these circumstances might throw some light on the defect in gout.

From the practical viewpoint it is important to question the patient specifically about gouty or rheumatic symptoms before prescribing oral diuretics. Equally the significance of such symptoms, which need not necessarily take the form of a classical attack of gout, should not be overlooked if they occur while the drug is being taken. They will usually subside quickly once treatment is stopped, but if a gouty diathesis has been revealed in this way the administration of uricosuric agents such as probenecid may have to be considered.

[1] Warshaw, L. J., *J. Amer. med. Ass.*, 1960, **172**, 802.
[2] Aronoff, A., *New Engl. J. Med.*, 1960, **262**, 767.
[3] Price, N. L., *Lancet*, 1939, **1**, 22.
[4] Laragh, J. H., Heinemann, H. O., and Demartini, F. E., *J. Amer. med. Ass.*, 1958, **166**, 145.
[5] Oren, B. G., Rich, M., and Belle, M. S., ibid., 1958, **168**, 2128.
[6] Monroe, K. E., Grant, L. H., Sasahara, A. A., and Littman, D., *New Engl. J. Med.*, 1959, **261**, 290.

British Medical Association

ANNUAL MEETING, TORQUAY, 1960

SUMMARY OF PROCEEDINGS

THE SECTIONS

FIRST SYMPOSIUM—MODERN AIDS TO DIAGNOSIS

Monday, June 20

With Sir ARTHUR THOMSON (Birmingham) as chairman, a symposium on modern diagnostic aids included descriptions of the indications, value, limitations, and abuses of needle biopsy, of radiodiagnosis, of diagnostic virology, and of chemical pathology.

Needle Biopsy

Dr. J. G. HUMBLE (London) first stressed that needle biopsy was no new investigation, having been successfully used by Küss in 1847 to demonstrate carcinoma cells from a malignant tumour. The scope of the method had gradually grown until examination of tissue obtained by this technique was widely used in the diagnosis of disease of the liver, kidney, prostate, thyroid, lymph nodes, bones, pleura, bone-marrow, or indeed of any accessible individual mass of indeterminate origin. Further, fluid for cytological examination could be obtained by needle puncture from the pleura, peritoneum, and theca.

Experience of the examination of material obtained on 2,000 occasions had convinced Dr. Humble of the value of this method. As predominantly a haematologist, he had been mainly concerned with the interpretation of bone-marrow slides, and illustrated his remarks graphically by detailed reference to 17 patients in whom needle biopsy had materially aided diagnosis. Information was often obtained which confirmed the physician's clinical impressions, but on occasion totally unexpected findings had opened up new aspects of particular problems.

In reply to questions Dr. Humble said that liver biopsy yielded most information when diffuse liver disease was suspected, as in hepatitis or amyloidosis, or when the cause of a large liver had not been determined. The progress of reversible hepatic lesions, such as hepatitis or haemochromatosis, could also be assessed. Biopsy was less valuable in focal hepatic lesions such as sarcoidosis or neoplastic deposits.

Radiodiagnosis

In a thoughtful and witty address Dr. CHARLES WROTH (Exeter) surveyed the developments in diagnostic radiology in the 65 years following the discovery of *x* rays, and wondered if clinical wisdom had kept pace with the technical developments in the field. He doubted if the modern doctor was worthy of the wonderful heritage which Röntgen had left to him.

He felt the clinician was frequently at fault in his poor selection of patients for examination, by not knowing if the *x*-ray examination he required was technically possible or whether his patient was equal to it. Much unnecessary duplication of *x*-ray photography took place, and too often examinations were undertaken purely to protect the doctor from subsequent litigation. Radiodiagnosis was regarded by doctor, patient, press, and jurist as an infallible, universal, legally enforced procedure, and its costs were far more open to censure than the much-criticized prescribing costs. The only cure for such abuses lay in publicity and in education of patients and doctors alike, and by insisting that medical students worked for a short period in an *x*-ray department learning the difficulties, costs, and limitations of the procedures they would soon so glibly request.

In interpreting radiological reports, whether positive or negative, the doctor frequently failed to appraise them in the light of the clinical findings, and embarked on fruitless lines of investigation or treatment. The implications of the films and reports, and their reliability and relevance to an individual problem, called for much experience and judgment.

Dr. Wroth felt that most of the defects he had detailed resulted from lack of liaison and co-operation between clinician and radiologist, and thought that future generations of medical students should be educated to avoid this defect. He concluded his stimulating address by showing some films to illustrate that positive or negative *x*-ray findings were by no means infallible and were never a substitute for thoughtful diagnosis. When questioned on the value of mass miniature radiological surveys, Dr. Wroth felt the few cases of disease they demonstrated were of inestimable value, but that many patients were submitted to unnecessary unhappiness and worry when recalled for further examination because of minimal abnormalities or technical faults in their original films.

Diagnostic Procedures for Virus Diseases

Dr. J. A. DUDGEON (London) detailed the many recent advances in the diagnosis of virus diseases which had taken place in the last 30 years. In 1930 only a few centres possessed the expensive facilities necessary to culture viruses, procedures which depended largely on animal inoculation. In the decade between 1930 and 1940 culture of viruses in the growing chick embryo became possible, the method being improved after 1940 by the addition of antibiotics to culture media, thus limiting bacterial contamination. Newer methods of growing viruses in tissue culture were simpler, cheaper, and more accurate, and had led to the discovery of many "new" viral agents from human subjects, such as the cause of aseptic meningitis, acute respiratory disease, and acute exanthemata.

Three methods of approach were used in diagnostic virology. First, a direct examination might be made for the virus or its effect on surrounding tissues. This quickly performed method had a limited application in the diagnosis of smallpox, some acute exanthemata, and rabies. Secondly, attempts might be made to culture the virus, and this constituted the most important method of early provisional diagnosis. The virus was cultured in the embryonated egg, in suckling mice, or in tissue or cell culture, the use of monolayer cultures of kidney or amnion being most suitable. These methods had virtually eliminated the need for using expensive laboratory animals for viral culture. The virus in culture could then be specifically identified by the cytological changes seen in tissue culture, by examining for haemagglutination or haemadsorption, or by staining with fluorescent-labelled antibody. Thirdly, serum could be examined for specific antibodies, a retrospective method depending on the demonstration of an increasing titre of these substances; this gave essential confirmation of the diagnosis established by other methods.

Dr. Dudgeon's lecture was beautifully illustrated by slides relating to specific virus diseases.

Chemical Pathology

Dr. D. N. BARON (London) recalled that, although qualitative urinary examination had been practised through the centuries, biochemical tests were amongst the most recently developed diagnostic aids. He showed that at the Middlesex Hospital in 1920 only one biochemical test was performed for each six admissions of patients; this ratio increased to one per patient admission between 1925 and 1947 and had shown a progressive rise since that time till 1960, when each admission produced five and six chemical tests. He attributed this increase to the increased scope and scientific background of modern clinical medicine, the necessity for the biochemical control of therapy and progress of disease, and the rapid expansion of new laboratory techniques such as flame photometry, hormone assays, and plasma enzyme determinations.

Most biochemical laboratories were therefore overloaded with routine work, a process which limited research, caused

discontent among workers there, and might occasion dangerous inaccuracies or delays. Biochemical staffs, because of the much better pay and conditions offered by industry, proved difficult to find and to keep. The recent development of mechanized accurate automatic analysers and washing-up machines might form a solution, but the initial outlay was considerable. Mechanization seemed unavoidable, and would pay for itself in staff salaries saved.

Biochemical facilities, rightly, were now available in most parts of the country, since they could offer aid in an ever-expanding variety of medical conditions. However, these facilities were widely abused, many fruitless investigations being undertaken because of the lack of knowledge of their limitations and the uncurbed enthusiasm of junior staff. Such abuses could be checked by closer consultation with the chemical pathologist, and Dr. Baron also thought that all medical students should work in a modern laboratory to obtain a greater insight into the technical difficulties and costs of biochemical investigation. Reduced work would mean a better and more personal service, which should become more and more available to general practitioners, who had only recently started to benefit from it. Simple tablet and paper tests for urinary and faecal analysis were great advances, giving more accurate results and reducing laboratory work.

Dr. Baron saw a great future for chemical pathology, not only in diagnosis but in elucidating the nature and cause of disease and in the study of the dynamic chemical pathology of the cell.

Sir ARTHUR THOMSON (Birmingham) thanked the speakers for the clarity of their presentations and on their awareness, as laboratory workers, of the human aspects of their patients. He felt that modern diagnostic aids had refined clinical judgment even though they might have robbed the over-pompous senior physician of his once unassailable authority, now so often subservient to a piece of paper produced from elsewhere. He stressed the necessity for integrating laboratory investigations with clinical impressions; they should never be requested unless the patient was likely to profit from them.

GENERAL SESSION

Tuesday, June 21

The Mental Health Act—First Impressions

Dr. S. NOY SCOTT (Plymouth) opened his remarks from the chair with news of the death of Professor Alexander Kennedy (Edinburgh), who was to have read a paper, and the meeting stood in silence as an expression of sympathy. Dr. T. P. REES (London) acted in Professor Kennedy's place, and delivered a paper on the new Mental Health Act. He said that it was most welcome, being based on recommendations of the British Medical Association, some of which had first been put forward as long ago as 1926. One effect of the new Act was to abolish "mental hospitals" as separate entities; all previous legislation on the subject was repealed. Patients could now be admitted to any hospital, and detained there if necessary, provided a suitable ward was able to receive them. The new Act also covered provisions for community care (treatment at home), informal admission (replacing the old "voluntary patient" category), and compulsory admission.

On the subject of *community care*, Dr. Rees said that the number of patients going into mental hospitals was highest in the most civilized country (United States of America), with Britain second. There were 20,000 admissions in 1929, and 100,000 in 1958; but the tide was turning, chiefly because general practitioners now had better therapeutic resources in the form of new drug treatments and social services such as home helps, night attendants, meals on wheels, training centres for backward children and handicapped adults, etc. There was need for much more of this type of provision, especially hostels for those who could not manage a home but could do simple work, and more accommodation for the elderly. Regional hospital boards should provide improved out-patient facilities for treatment rather than offer a mere diagnostic service with referral back to the general practitioner or admission to hospital as the only disposals.

Informal admission was intended to cover all patients who did not actively object to going to hospital, and would probably account for 90 to 95% of admissions. *Compulsion* was necessary for the remainder. Dr. Rees thought it unwise to try to define the more severe states, and foresaw difficulties when lawyers began to apply the definitions in the Act.

Speaking of changes brought about by the Act, Dr. Rees said that the duly authorized officer could not now act alone, and the place of the magistrate in certification had gone. The new system required an application by the next of kin or by a mental welfare officer to be supported by two medical applications (one in emergency). Subsequent release from hospital could be ordered by the medical officer concerned, by the next of kin, by three members of the management committee, or, if all these failed, by appeal machinery.

Dr. Rees concluded by asking for full co-operation between the general practitioner, hospital doctor, and medical officer of health. Failing this, the patient would suffer.

In response to a question from Dr. F. STEEL (Finchley, London) Dr. Rees described the means of detaining for three days an informally admitted patient who wished to discharge himself but was deemed unfit to do so, and for Dr. A. BARKER (Whitstable) he estimated that it might be ten years before there was an adequate number of home helps, night attendants, etc., to make community care equal to its task.

Trends in the Incidence of Cancer

The Director of the South-western Regional Cancer Records Bureau, Mr. REGINALD M. VICK (Broxbourne), placed copies of the 1958 annual report of his bureau in the hands of the meeting, and described how it was compiled. A population of nearly three million was covered, an excellent number for statistical work, and he had recorded over 84,000 cases of cancer. The World Health Organization's classification of disease was used to make the figures comparable with those of other workers. The reports were circulated annually to interested persons. A bias was maintained towards clinical presentation so that changes in incidence and assessment of results of treatment were more easily seen from the tables. There was evidence that the report was widely used and valued, and that some other regions were developing their own bureaus to do similar work. Hospital notes seemed to be improving in quality, apparently because of the interest shown by following up the cases. General practitioners co-operated well, but occasionally surgeons seemed to lose interest as soon as they had completed their operative treatment. Since 1954 the Registrar-General had provided details of cancer deaths, and these had been a valuable check on the registered figures.

Mr. Vick went on to instance certain kinds of cancer which showed special features. Cancer of the lip was mainly a man's disease (235 males against 20 females). Ten-year survival rates were presented for the first time, and showed that cancer of the stomach was very dangerous (5-year survival rate 12%—10-year rate 8%), colonic cancer not quite so bad (32%—25%), breast cancer, stage I, fairly good (63%—40%), and stage IV, bad (6%—2%). Cancer of the uterus (62%—41%) was responding to modern treatment with improved results (latest figure 82% survivors), as were some of the other types of cancer; and malignant melanoma was not so fatal as had been supposed (45%—33%).

A brief analysis of the tables of incidence and virulence of different sorts of cancer showed that the incidences of breast and lung cancer were both high, but their killing powers were different, so that many more deaths occurred in the follow-up period from lung cancer. Mr. Vick also

showed, by comparison of figures from different sources and years, that the incidences of cancer of various organs, relative to each other, changed little.

After deploring the absence of recording bureaus in some parts of the country, Mr. Vick concluded by stressing the care with which records were handled, and paid a tribute to his office staff. In reply to a question from Mr. MALCOLM DONALDSON, Mr. Vick said that the Ministry had tried hard to persuade other regions to start cancer records bureaus, with scant success. Another question, from Dr. A. K. PITTMAN (Horsham), elicited Mr. Vick's opinion that death certificate diagnoses were in many instances unreliable, and sometimes quite unusable, but the follow-up system often derived better information. He reassured Dr. T. W. DAVIES (Swansea) that the form of return used was not a difficult one—it could not be so, or busy doctors would have neither time nor inclination to complete it.

Migraine

Dr. RAYMOND GREENE (London) delighted the audience by projecting a diagram of an elephant undergoing palpation by a number of blind men, each hotly contending that his own version of the truth was the right one. The situation was described in verse, the point of which was that fluid balance was only one of a number of approaches to the problem of the aetiology of migraine. Dr. Greene then detailed the changes in water and sodium content which accompanied attacks, with comparisons with those which accompanied menstruation. There was usually water retention for five days before the menstrual flow began, at which time diuresis occurred. Water and sodium balance were connected in many cases with migraine attacks; but if temporary water retention caused migraine, what was the cause of temporary water retention? Relief of water retention did not always relieve migraine, nor did production of water retention always result in an attack. Water retention was not therefore a cause but a predisposing agent.

Dr. Greene, who had been introduced as having been a panel doctor for ten years at the beginning of his career, gave as his final opinion that if ever there was a disease which was for the general practitioner to treat, rather than the specialist, it was migraine. If a specialist had to be called in, he should be selected with care. Every patient needed careful study to determine what triggered the attacks, and there was nearly always some such trigger. It was easier for the patient's family doctor to find it than for the consultant; for it might take prolonged study of the patient, his home, his work, and his environment in general, before the trigger could be found.

In response to questions, Dr. Greene decried the value of desensitizing injections. These were expensive and often ineffective. If the patient got an attack every time he consumed porridge, his best answer was to stick to corn flakes.

DEBATE

Wednesday, June 22

Telling the Public about Medicine

"That dissemination of medical knowledge by means of television, radio, and the press does more harm than good to the health of the population"

was the motion before the House at the Debate on Wednesday, June 22. The proposers were Dr. LINDSEY W. BATTEN (Hampstead) and Dr. MYRE SIM (Birmingham), and the opposers were Dr. JOHN FRY (Beckenham) and Professor L. J. WITTS (Oxford). The chair was taken by Dr. R. M. S. MCCONAGHEY (Torquay), who explained that the debate was a new departure at an Annual Meeting. It was an opportunity for a free expression of views on the subject, but he pointed out that the result of the vote at the conclusion of the debate should not be taken as representative of any official opinion of the Association.

In opening, Dr. MYRE SIM recalled that in a survey conducted by the B.B.C. it was estimated that the number of persons who saw the programme "Your Life in Their Hands" was some 8½ million. The most popular of that series was an operation on the liver and the next in popularity was an operation on the heart. The least popular was the work of a cottage hospital in Cornwall. That was not surprising, said Dr. Sim, because it was the least spectacular and dramatic. He questioned whether the public were being educated by such programmes.

Although it was appreciated that medical publicity could do good—for instance, in the field of public health—Dr. Sim said he could not believe that it was good doctoring to broadcast to millions about the diagnosis of illness and its treatment—in some cases advocating drastic treatment—when the broadcaster had not seen those people and knew nothing of them. "What would an executive council say of a general practitioner who diagnosed a patient's illness and prescribed treatment without examining him?" concluded Dr. Sim. "Yet that was done in the case of some 8½ million potential patients, some of whom actually suffered from disease. I find that very difficult to accept."

Doctor–Patient Relationship

In opposing the motion, Dr. JOHN FRY referred to the doctor–patient relationship, and said that the most serious criticism was the suggestion that education of the public by press, television, and radio was causing great harm in the relation between doctor and patient. The implication was that any such education should be a monopoly of the doctor. The doctor presumably would decide what his patient should or should not know. The criticism also implied that the doctor–patient relationship was so slender that it might be shattered if the patient knew too much. What rubbish! said Dr. Fry. It would be strengthened, he suggested, if the patient came along and discussed with his doctor the matter he had heard or read about and sorted out his problem with the doctor. "The essence of good general practice is surely to encourage our patients to come to us for advice and discussion however seemingly trivial their complaints," he said.

Society of Secrets

A considerable proportion of the profession was against telling the patient anything, with the result that the profession had become a gigantic society of secrets, and medical practice had tended to become shrouded with mysticism. At the same time, efforts had been made to rationalize types of medical care and methods of educating students. More people were becoming better educated now, with the result that the doctor no longer enjoyed the prestige of being one of a small number of educated people in a community. Mysteries of medicine were no longer accepted blindly. "The public is thirsty for information on all matters, and particularly information concerning medical matters," continued Dr. Fry. "It may be a morbid fascination as the *British Medical Journal* has pointed out, but it is something that the public want, and if we do not give it to them they will get the information somewhere."

Dr. Fry suggested that the medical profession must accept the challenge of educating and informing the public, and to do so co-operation was necessary. To achieve the best results between the profession, the producers of programmes, and writers in the press, the Council of the British Medical Association should form a liaison committee to link the various bodies. The public wanted to be medically educated, and it was up to the profession to ensure that such education was always of the best type.

The Trumpet's Uncertain Sound

Dr. LINDSEY W. BATTEN, supporting the motion, suggested that what the public wanted and what the disseminating organs liked to give them were views and news and knowledge, not of what the medical profession knew but rather of what they were doing. When it came to news, the formidable fact was that the profession could never agree

about anything, and it was doubtful whether it was a good thing that the public should know that. "The simple folk we are talking about look at television, and it will take a lot to teach them that what we say so confidently to-day will be untrue and even dangerous to-morrow," he added. Dr. Lindsey Batten recalled that not so very long ago it was sound medical practice that babies should be fed every four hours, but now there was the so-called "demand schedule," which meant that they were fed when they were hungry. Again, the profession could not make up their mind whether the breast was better than the bottle or vice versa—"If the trumpet give an uncertain sound, who shall prepare himself for the battle," he said. The medical trumpet was always giving an uncertain sound.

Referring to drugs, Dr. Lindsey Batten said that the profession were always having to change their mind about drugs which they thought were heaven-sent and which turned out to be very dangerous. The latest discoveries should never be broadcast, for there was a danger that it would bring the medical profession into disrepute.

If it could be shown that the dissemination of medical knowledge were good for the health of the public, Dr. Lindsey Batten said he wondered whether the best doctors would be on the platforms, writing to the press and appearing on television to disseminate that knowledge.

On the question of the effect on those who viewed or listened to medical programmes and whether it did them any good to have medical knowledge disseminated, he suggested that members of the profession themselves were fairly good guinea-pigs. They possessed knowledge as a profession, but how much good did it do them? Doctors were not all that healthy. They did not live longer than their brethren in the Church who knew much less medically, and insurance companies did not consider doctors to be "good risks." If anything it was rather the reverse.

Dr. Lindsey Batten said he was afraid that a race would be bred of "viscera viewers" with no sensibility at all, and one which would be subservient to doctors—a race which could not move a hand or foot without asking the doctor. "I want health to prevail," he concluded. "I am sure it is our duty to spread useful knowledge to our patients; but I am also sure that we should do it at the bedside, in the clinics, and in the consulting-room, and not on the platform."

A Matter of Taste

Professor L. J. WITTS, opposing the motion, said it was perfectly normal for people to be interested in birth, death, disease, and disaster. They needed to know about health and disease as they needed to know how to read and write if they lived in a modern community. The question was largely one of good taste and was not a matter of condoning bad methods of medical publicity. Apart from preventive medicine, there was a need to explain to the public how costly were drugs, *x* rays, and new scientific apparatus. Blood donors were needed, as were first-aid workers and recruits in all branches of the Service—recruits who were not coming forward in sufficient number at present. Co-operation of patients in research was required, and an understanding by the public of problems of research with respect to human beings and animals. The first rule of clinical research to-day was that it could only be done with the voluntary consent of the patient, and for that it was necessary to have an informed public.

It was only justifiable to maintain medicine as a mystery when patients could feel that they were not only in their doctors' keeping but also in God's keeping. With the wide-spread decline in faith, the medical practitioner's task had become more difficult.

It should be realized that the dissemination of knowledge was a two-way process; it had a feedback mechanism. Medicine was much too important to be run by doctors. It was important that lay people should have a proper knowledge of medicine, because all professions suffered from occupational diseases, and a little publicity was very good for them.

Art as Well as Information

Methods of presentation should differ according to the size of the audience being addressed. The larger the audience, of course, the less complex were the ideas which could be put over. The radio talk or television programme on a medical subject was not only a piece of information but should also be a piece of art, and if more care were taken with the art, the information would take care of itself.

Professor Witts suggested that the standard of public hygiene in the United States, which was infinitely better than in Britain, was in part due to the dissemination of medical knowledge, and it would be desirable if this country were educated to the same standard.

In his view nothing could stop the public's interest in medicine, and nothing could stop the use of mass media to satisfy it. "If the dissemination of medical knowledge by these media at present is wrong, then it is an indictment of us as a profession," he concluded. "I do not think it is doing harm, although I think that it can be done a great deal better. There is no evidence that it does significant harm, but there is considerable evidence that it does good, and much to suggest that it could do even more good."

In the subsequent debate from the floor, Mr. MALCOLM DONALDSON (Oxford) referred to the object of cancer education, which, he said, was to give the public knowledge of early diagnosis and to get rid of fear. "This conspiracy of silence causes great delay in the diagnosis and treatment of cancer," he said. Knowledge was the antidote to fear, and cancer education needed the assistance of publicity. He would vote against the motion.

Dr. R. A. BLAIR (Manchester), a psychiatrist, agreed that psychiatry had benefited from the widespread dissemination of general knowledge about the medical situation, but said he felt on balance that present trends were inclined to be harmful. There was a difference between learning and knowledge. True knowledge was never harmful, whereas learning could be.

Dr. W. N. LEAK (Cheshire) said that in his experience the dissemination of medical knowledge had, on the whole, amounted to health education, and had done his patients good. It could remove fear, and that was, in itself, health-giving.

Dr. ELSIE WARREN (Kensington) suggested that if television had been available fifty years ago, lives would have been saved and much good done so far as midwifery was concerned.

Dr. J. BALLANTINE (Coventry) said it was difficult to see how it was proposed to stop the dissemination of medical knowledge by television and the press. The job of the profession was to see that the knowledge was disseminated properly.

An Artificial Demand

Dr. S. NOY SCOTT suggested that if there had been a demand for the dissemination of medical knowledge it was an artificially stimulated demand. In his view it was morbid sensationalism. Premature publicity so far as insulin and cortisone were concerned had done a great deal of harm, and Dr. Noy Scott said he was not convinced that if the public dissemination of medical knowledge were continued it would necessarily be done by the best doctors.

Dr. DAVID STAFFORD-CLARK said that anybody who had participated in the dissemination of knowledge of any kind must have done so because they thought the information which they were disseminating was worth while. There was not only interest in the programmes but a great deal of ignorance and fear to be dispelled. To give the public the kind of information which would enable them to form a judgment about what was reasonable and what was expected from doctors was not likely to do harm.

Dr. ALISTAIR R. FRENCH (Marylebone) urged those present to vote for the motion, bearing in mind that present methods of disseminating medical knowledge should be controlled to such an extent that it did not do harm.

The Chairman then put the motion to the meeting, and on a show of hands it was lost by 44 votes to 43 votes.

SECTION OF MEDICINE

Tuesday, June 21

Medical Treatment as a Cause of Disease

With Dr. A. H. DOUTHWAITE (London) as chairman, the role of medical treatment as a cause of disease was discussed by a distinguished panel of contributors. Putting the physician's point of view, Professor C. BRUCE PERRY (Bristol) reviewed the production of organic or psychological illness by the use of drugs, by physical agents, or by the behaviour of the doctor. He said that toxicity might develop because a drug was administered in too large a dose, for a prolonged period, or because of disregard of the safeguards necessary for its administration. An abnormal response or idiosyncrasy to a drug was an unpredictable hazard of varying and frequently indeterminate origin. The hepatic necrosis following cincophen treatment or the macrocytic anaemia induced by anticonvulsants were examples of this alarming phenomenon. In some instances a genetically determined enzyme defect might explain an individual reaction to a drug, as in the haemolytic anaemia accompanying primaquine administration.

Many drug diseases resulted from sensitization such as serum sickness, thrombocytopenia, purpura after "sedormid" (apronal) or allergic reactions induced by sulphonamides or thiouracils. So called side-effects of drugs frequently induced symptoms or disease, as in osteoporosis of prolonged steroid administration, the depression accompanying rauwolfia compounds, or the emergence of resistant organisms after antibiotic therapy. Frequently a new disease might be caused, unmasked, or exacerbated when a particular illness was being treated, such as the Parkinsonism produced by chlorpromazine, or the central or renal ischaemic damage which followed overenthusiastic hypotensive therapy.

Irradiation too had also produced an appreciable morbidity and would probably increasingly exert its effects, as in the leukaemia which had followed *x*-ray treatment of spondylitis or even minimal exposure to radiation in childhood. The usage of substances normally essential and beneficial in small dosage might be dangerous in excessive concentration, as in the blindness produced in premature children after oxygen therapy or nephrocalcinosis produced by the enthusiastic administration of vitamin D in infants. Infectious diseases might also be spread by the doctor, as in syringe-transmitted hepatitis, in contaminated eye-drops, or by the unrecognized transference of resistant organisms in the physician's nasopharynx. Much psychological illness was caused by something the doctor had said or done or by his ill-advised handling of the illness. Doctors must therefore restrain themselves in prescribing potentially dangerous drugs for trivial ailments and from incautious or injudicious statements about their patients' health.

Too Early Treatment

Speaking as a dermatologist Dr. J. R. SIMPSON (Exeter) first decried the tendency to prescribe a drug early, rather than to wait for the natural evolution of the disease or even before establishing a precise diagnosis. He particularly condemned the unnecessary use of *x* rays in dermatological conditions where much simpler and safer measures were available.

Skin reactions to ingested drugs were of all types and rarely specific. The fine punctate petechiae which followed carbromal injection or the recurrent localized drug eruption which followed administration of phenacetin or phenolphthalein might be easily identifiable. Granulomatous, necrotizing, nodose, or photosensitivity eruptions all accompanied drug injections. He illustrated many of these conditions with beautiful coloured slides.

Eruptions produced by local sensitization to topical applications were equally common; picric acid, iodine, sulphonamides, neomycin, tar preparations, and local anaesthetics were common offenders. Generalized eruptions and intoxications might follow drug absorption from a cutaneous surface, such as the mercury poisoning produced after repeated application of the ointment in psoriasis.

One disadvantage of modern treatment of skin conditions by antibiotics and by steroids was their power to suppress signs and symptoms, temporarily encouraging the physician to abandon his search for a specific cause or so modifying the disease as to make its recognition difficult. Here again handling of the patient was extremely important, as an excessively gloomy prognosis or the possibility of legal action might exacerbate a constitutional tendency to worsen the disease.

Psychiatric Advice

In the clinical practice of psychiatry Dr. D. STAFFORD-CLARK (London) considered that there were three ways in which medical treatment might cause, contribute to, or worsen disease. Firstly, by an incorrect or unsympathetic attitude of the doctor to his patient. He particularly regretted the use of such phrases as, "There is nothing wrong with you," "Pull yourself together," or, "It is all up to you," in a patient whose attempts to do so had already completely failed. Such statement belied patience or compassion and frequently so undermined confidence in medical help as to render suicidal attempts possible. The speaker vehemently condemned medical advice to "keep away from psychiatrists" as offensive, unreal, and verging on negligence, an attitude of mind which resulted from complete ignorance of the advances made in modern psychiatry. Secondly, disease might be caused by the medicinal measures prescribed. Phenobarbitone, though an excellent drug in mild anxiety states, epilepsy, and migraine, was dangerous in depressives. Bromides should never be used, as the cumulative intoxication they produced would simulate organic confusional states. Paraldehyde injections, regarded in many quarters as a safe hypnotic, were in fact slow-acting, inefficient, painful, and often dangerous, and would only serve to frighten, hurt, and impair contact in an already disoriented subject.

Finally, disease might be caused by the actual treatment given, whether surgical, medical, psychiatric, obstetric, or environmental adjustment. Dr. Stafford-Clark particularly cited the lack of explanation to the patient before major surgery was undertaken.

Rare Cause of Death

The pathologist had the last word when Dr. J. W. LANDELLS (London) cheered his audience by finding that in only 0.5% of 4,000 necropsies at a London teaching hospital was death attributable to iatrogenic illness. This figure excluded gross technical blunders, misadventure of hazardous operations for serious disease, acts of omission or delay by the doctor, or where the patient was already ill before coming under the doctor's care. He thought that, while it was fair for the profession to scrutinize its actions critically, fear of the outcome of therapy must not prevent the physician from using his most powerful armament as quickly when required.

Unpleasant complications to treatment were far more commonly induced than fatalities; unnecessarily vigorous or prolonged therapy, irradiation, steroids, and drugs incompletely assessed therapeutically being the commoner causes for their production.

The profusion of newly introduced drugs made it necessary to instruct medical students in the critical appraisal of remedies and in knowing when to stop them. Dr. Landells ended by stating that he did not feel that the standard of care shown by the profession should be recklessly questioned by the imputation that serious disease often resulted from doctors' actions. He told his audience that in his necropsy experience a patient was four times as likely to develop cancer twice as to be killed by his doctor.

In subsequent discussion reference was made to the value of marking the notes of patients who had shown drug reactions or who were taking steroids. Professor SHEILA

SHERLOCK stressed the serious prognosis of the hepatocellular damage produced by iproniazid, but Dr. Stafford-Clark felt the risks of suicide in an untreated depressed patient far outweighed the chances of possible liver damage. The difficulty of knowing what the patient was taking was referred to by several speakers, and a plea made for the inclusion of this information in notes or letters of referral.

Wednesday, June 22

Malabsorption Syndrome

At the meeting of the Section of Medicine, with the president, Dr. A. H. DOUTHWAITE (London), in the chair, distinguished speakers read papers on the malabsorption syndrome, on the chemotherapy of malignant disease, and on recent trends in diabetic research and therapy.

Dr. R. H. GIRDWOOD (Edinburgh) felt the term malabsorption syndrome was not wholly appropriate, as the clinical features of patients included in this definition varied greatly. He thought that the three advances which had contributed most to the knowledge of the syndrome were studies of folic acid metabolism and of the role of gluten in its production, and the histological examination of jejunal biopsy material.

In proposing a classification of malabsorption states, Dr. Girdwood considered that as the relationship between coeliac disease of infancy, adult coeliac disease, and tropical sprue was uncertain he preferred to call them "gluten reactive malabsorption of infancy and childhood," and "primary malabsorptive disease of the adult" and "of the tropics" respectively. He recalled that similar syndromes might result from intestinal mucosal atrophy after malnutrition, chemical or irradiation damage, from structural disease of the small intestine or mesentery, from the blind-loop syndrome, after gastric operations, and in pancreatic deficiency.

In appraising the value of jejunal biopsy he said that partial or complete villous atrophy usually accompanied primary malabsorption disease but that rarely normal mucosal appearances were seen. He had been unable to correlate the clinical features of the malabsorption state with the type of mucosal change. Studies in the absorption of folic acid and cobalt-labelled B_{12} were reported in large series of control subjects and patients with malabsorptive states, in which the site of the lesion in the gut often determined whether a particular agent would be absorbed normally. Dr. Girdwood had shown that bacteria isolated from blind loops of intestine at operation took up cyanocobalamin, arginine, lysine, leucine, and isoleucine from culture media, and in this way might deplete the living patient of these and other substances.

In discussing the absorption of carbohydrate, fat, and protein in health and disease Dr. A. M. DAWSON (London) first illustrated the problems in studying intestinal absorption by reference to the glucose-tolerance test. This gave a composite picture of the rates of gastric emptying, of absorption, of tissue utilization, and finally of renal clearance of carbohydrates. It was hard to devise tests of absorption where all these factors were known, balance tests based on the faecal excretion of the compound being most suitable.

Fat prior to absorption was digested by pancreatic enzymes entering the intestinal mucosal cell as a split fat, where it was resynthesized to neutral fat, then passing into the local lymphatics. Intubation studies had shown the rapidity of action and potency of lipase in the pancreatic secretions, up to 50 g. of dried pancreatic extract being necessary to produce a similar effect. Bile salts acted not only by emulsifying fat in the lumen of the gut but also by exerting a direct stimulating effect on the mucosal cell to resynthesize neutral fat. Here again large amounts of bile salts were necessary to ensure effective fat-absorption, up to 100 g. daily being necessary to replace a total deficiency. The failure of oral bile salts to correct steatorrhoea in liver disease was due to inadequate dosage and the fact that commercial preparations contained impurities which were toxic to the mucosal cell and induced vomiting and diarrhoea.

Proteins were also rapidly hydrolysed by the pancreatic enzymes in the gut prior to absorption, and impaired mucosal function might be associated with their defective absorption. However, this could not account for the low body stores of protein seen in such patients, for the basic nitrogen requirements in man were much lower than was usually taken in the normal diet. A likely factor in protein depletion, which had been shown to be of importance in the so-called "protein-losing enteropathies," was the leakage of protein from the blood-stream into the lumen of the diseased bowel.

Chemotherapy of Malignant Disease

In describing agents used in the chemotherapy of malignant disease Dr. J. INNES (Edinburgh) discussed the development of these compounds during the last 100 years, when arsenic had first been used to treat chronic myeloid leukaemia. Overall success had been disappointing, and no real cure had been achieved. Agents used fell broadly into two groups: the radiometric cytotoxic agents, which had produced temporary improvement in widespread reticulosis, and secondly the group of antimetabolite and steroid compounds which had induced remissions in children with acute leukaemia and produced results comparable to irradiation in adult chronic leukaemia. No chemical compound had yet proved really effective against tumours arising from epithelial tissues, and as a result the main challenge of neoplastic disease was relatively untouched.

All chemotherapeutic agents damaged normal as well as neoplastic cells, and frequently produced bone-marrow depression. This made regular blood counts throughout treatment essential, and was the limiting factor in continued dosage. Attempts to destroy epithelial tumours by massive dosage of antimitotic agents followed by marrow replacement or local perfusion of tumours by alkylating agents were promising advances in the field but still extremely hazardous procedures.

In assessing any chemotherapeutic compound, its value in the light of the natural history of untreated disease or the results obtainable by irradiation should be studied over a long period. He felt the main hope in cancer chemotherapy lay in the development of antimetabolite compounds or in the recognition of an enzymatic deficiency which might affect the fundamental growth processes of neoplastic cells.

Recent Trends in Diabetic Research and Therapy

Professor W. J. H. BUTTERFIELD (London) reviewed recent developments in research and therapy in diabetes. By a technique developed in his laboratory at Guy's Hospital the carbohydrate metabolism in the forearm tissues in normal and diabetic subjects had been studied. Contrary to current expectations, it was shown that the peripheral tissues had a glucose threshold which had to be exceeded if glucose was to shift from blood to tissues. In normal subjects the fasting blood sugar approximated to the tissue threshold, which could be raised by oral glucose and lowered by insulin. In diabetics both tissue threshold and blood sugar were greatly elevated, and glycosuria occurred when the renal threshold was exceeded.

The implications of these findings were discussed in relation to the two main types of diabetic subject—namely, the juvenile diabetic, who had a serious insulin deficiency, and the more elderly one in whom the deficiency was only a relative one.

Professor Butterfield then reviewed the mode of action, indications, and efficacy of oral hypoglycaemic agents, reminding his audience that such compounds were no new developments, as the hypoglycaemic effects of salicylates had been known since 1877. It had been shown that these compounds could lower the glucose threshold of the peripheral tissues, but that in addition the sulphonylureas were thought to stimulate insulin production and the guanidines to augment the action of the reduced amounts

of insulin available. The selection and treatment of suitable diabetic subjects with oral hypoglycaemic agents were considered.

The speaker concluded by emphasizing that effective diabetic control demanded from the patient his adherence to diet and treatment, from his family their help to the patient and their vigilance in the detection of latent cases amongst them, and from the doctor the careful supervision of therapy. Research workers and pharmaceutical companies should concentrate on investigating mechanisms, complications, and treatment of diabetes, and lay organizations and public-health authorities should supervise the welfare of diabetics and the dissemination of knowledge among them.

SECTION OF SURGERY

Tuesday, June 21

Economic Aspects of Surgical Treatment

With the president, Professor R. MILNES WALKER (Bristol), in the chair, the discussion on economic aspects of surgical treatment was opened by Mr. A. DICKSON WRIGHT (London).

A commercial undertaking, not running efficiently, Mr. Dickson Wright said, would call in an independent efficiency expert, and the substance of his paper was a report by this mythical medical inspector, whose first task would be to overcome the natural reluctance of surgeons to agree to any sort of direction. After examining the length of stay of patients in hospitals he would have to consider the difference in results of treatment by two classes of surgeon, the learning and the taught. He would be struck by the fact that the former, frequently from abroad, was doing a very large amount of operative and clinic work, and often unsupervised. He would regard this as uneconomic, and would recommend more money to be invested in training and for visiting other centres. There should be more apprenticeship at teaching hospitals and less self-teaching at the periphery.

The inspector would look to the steeply rising cost of ancillary investigations, and would conclude that extravagance had greater risks than had economy in surgical treatment. He would certainly reduce the waste in blood transfusion, antibiotics, and pathological tests "ordered by juniors and not read by seniors."

Too Expensive Equipment?

Mr. E. L. FARQUHARSON (Edinburgh) was unfortunately unable to be present because of illness, and his paper was read for him. He too was critical of the rising costs of hospitalization, and laid much of the blame on surgical shoulders. Did expensive equipment, such as theatre lamps costing £400, really lead to better surgery? Did the air-conditioning plants now being installed at vast expense really diminish the risks of cross-infection? Ten years ago he had started operating on patients with herniae as out-patients, not primarily as a measure of economy but in order to reduce the waiting-lists. A film was shown demonstrating the methods employed. He had operated on about 550 patients in this manner, and, although he could not say what the cost to the country had been, at least the sum saved at an average of £25 a week per in-patient must have been considerable.

High Cost of Treating Children

Professor A. W. WILKINSON (London) said that the cost of maintaining children in hospital was relatively higher than adults. This was in part due to the high nurse–patient ratio, which at the Hospital for Sick Children was 1.23 to 1. The cost per patient might vary from as little as £6 for a hernia case admitted on the day of operation and discharged the following day to £400 or more for a child who had to be in hospital for three months. Individual apparatus—for example, a Spitz–Holter valve for the treatment of hydrocephalus or an adjustable spinal brace—was expensive to the hospital, but the cost of shoes to the parents of a child born with feet of unequal size might be just as great. Fortunately some manufacturers were prepared to supply pairs of shoes of different sizes. Professor Wilkinson made a plea for treating neonatal congenital abnormalities in a few properly equipped centres.

Housewives First Back to Work

Mr. A. M. N. GARDNER (Torquay) described an investigation he had conducted concerning the loss of working time in patients operated upon for (1) appendicitis (without complications), (2) hernia, and (3) haemorrhoids. The four groups he compared were (1) housewives, (2) employed males, (3) employed females, and (4) self-employed males. He also compared these groups with somewhat similar American figures. After all three operations it was the housewives who were first to go back to work (though even they were consistently beaten by the U.S. Air Force); and it was the self-employed males who took the longest time off work. His conclusion was that in the Welfare State it should be made worth while for everyone to work all the time: at present many people lose little, and some even gain from periods of idleness.

Hyperparathyroidism

A short paper on "Atypical Presentation of Hyperparathyroidism" was given by Mr. W. M. KEYNES (London). For practical purposes, kidney stone or disease of bone, both complications of primary hyperparathyroidism, were needed to call attention to the disease. It was nearly 70 years since von Recklinghausen described generalized osteitis fibrosa cystica, and more than 10 years later that a parathyroid tumour was found to be associated with this disease. However, it was only 25 years since the association of renal lithiasis with hyperparathyroidism was observed and that such stones could occur in the absence of any bone changes. Mr. Keynes analysed 175 cases from the Massachusetts General Hospital, 69% of which had renal stones. It was probable that about 5% of kidney stones were caused by overaction of the parathyroids. A variety of bone diseases, likewise, might result from this same cause, and some were labelled giant-cell tumours or an epulis of the jaw. Anaemia and leucopenia might be caused by the associated bone-marrow fibrosis. There were also other far less tangible ways in which hyperparathyroidism presented: peptic ulceration, chronic pancreatitis, adenomata involving several of the endocrine glands, and rather vague symptoms associated with the hypercalcaemia such as lethargy, polyuria, polydipsia, and visual disturbances. Exploration of the neck was required in the majority of patients to demonstrate the parathyroid adenoma (sometimes all four glands being affected), the tumour or tumours seldom being palpable.

Masses in the Neck

After tea, the president introduced Professor ISIDORE COHN (New Orleans, U.S.A.), emeritus professor of clinical surgery in the University of Louisiana, who paid tribute to a number of British surgeons and anatomists in regard to the understanding of masses in the neck. He outlined the very large number of conditions, congenital and acquired, which might be encountered, and deprecated the "flippant manner" in which they were so often regarded by clinicians. He did not wish to delve too deeply into embryology, but described the interesting hygroma colli (cystic hygroma, lymphangioma) which had a common developmental origin with the jugular vein and in which a lymphatico-venous fistula was present. Thyroglossal cysts always had a track which passed through the substance of the hyoid bone, and it was therefore necessary to bisect and core out this bone in following the track to the base of the tongue. In spite of such a radical procedure, repeated operations were sometimes necessary.

The rare and fascinating carotid-body tumours were described in some detail. Excision was the only treatment, and this often entailed ligation or excision of one or more

of the carotid arteries, a risk which could be more easily accepted since arterial grafting became possible. Lastly Professor Cohn touched on some of the constitutional causes of cervical lymphadenopathy, inflammatory and neoplastic.

Lumps in the Thyroid

Mr. ROBERT V. COOKE (Bristol) confined his remarks to lumps in the thyroid gland, some of the most important of which were in fact not truly lumps because they were impalpable. Advanced primary thyrotoxicosis was an example in which the gland might even be smaller than normal, but more often the enlargement was impalpable because the gland was wrapped round the postero-lateral aspects of the trachea and oesophagus. Some excellent slides illustrating this were shown, wtih others showing how outlying portions of the gland might escape detection at operation. The point was made that malignant disease of the thyroid often occurred in the solitary nodule, was insidious in onset, and affected a young age-group, even children. It was therefore easy to overlook. Mr. Cooke ended with a consideration of the three forms of thyroiditis.

Wednesday, June 22

Cross-infection in Operating Theatres

For the second session two vice-presidents of the Section presided, Mr. G. E. LARKS (Plymouth) and Professor H. W. RODGERS (Belfast). The opening paper was by Dr. W. A. GILLESPIE (Bristol), who restricted his observations to infection acquired at operation. Staphylococci and the Gram-negative bacilli were the chief villains, the latter especially in theatres used largely for urological work. In addition to the tissues obviously at risk, such as the subcutaneous tissues, joints, and the urinary tract, modern surgery increasingly exposed the brain, heart, and great vessels to infection. Prevention depended on the recognition of the sources and modes of spread of organisms. The former could be divided into those within the theatre and those brought into the theatre from outside. A particularly important source was from instruments which could not be sterilized for certain, such as cystoscopes. In a urological unit the incidence of infection had been reduced from 80% to 8% by effective sterilization methods combined with disinfecting the urethra. Nasal carriers of staphylococci could be eliminated by nasal disinfectant creams and hexochlorophane baths over prolonged periods. It was perhaps asking too much that this should be universally applied, but it was certainly worth while in the members of a cardiac surgery team. The commonest source of infection from outside the theatre was the wards. The pre-operative bath could be a danger if the bath-tub had been previously used by a post-operative patient with infection, and hexochlorophane should always be added to the bath water. Crude grey wool and cardboard cartons were likely sources of clostridial spores.

Dr. R. BLOWERS (Middlesbrough) spoke of the dangers of punctured gloves. He described some very careful investigations using phage-typed staphylococci from surgeons' hands and infected wounds. He had confirmed that 30% of gloves were punctured at the end of operating and after 200 operations half of the four chief gloves (i.e., those of the surgeon and his assistant) were holed. It was not, as generally supposed, needle pricks which caused punctures but the shearing strain of blunt finger dissection, pulling on retractors, or wringing out packs. He called attention to the inefficiency of the conventional method by which a nurse tests a glove for a leak by inflating only the fingers of the glove with air and "listening" for leaks. No schoolboy would be content to test a bicycle tube in that fashion and the whole glove should be inflated under water. He demonstrated convincingly how the older-fashioned latex-covered glove resisted puncture by a pencil point very much better than the modern solution-dipped glove. Another source of infection was the wetted sleeves of operating-gowns through which bacteria from the surgeon's forearms could readily pass. Bacteria-proof sleeve material was being developed to combat this risk.

Dr. E. J. L. LOWBURY (Birmingham) dealt with methods of sterilizing the hands and skin. Controlled experiments showed that, of various methods of scrubbing up, hexochlorophane ("phisohex") and 70% alcohol and chlorhexidine ("hibitane") were most effective in the prevention of this emergence of staphylococci through perforated glove fingers. The same benefit could be produced by the use of glove powder containing 5 mg. each of neomycin and of bacitracin per gramme of powder. The use of hexochlorophane soap for all ward ablutions was recommended. Six ways of pre-operative skin preparation were examined. Iodine in spirit had stood the test of time as well as of the present investigation, but sensitivity did occur and aqueous chlorhexidine was as effective.

Cancer of the Bladder

In considering the epithelial tumours arising from the transitional-celled epithelium of the urinary tract, Mr. ASHTON MILLER (Bristol) stressed that the concept of a division into benign or malignant did not apply as it might elsewhere. All were potentially malignant, but a tumour retained its specificity over the years. Tumours were almost unknown below the age of 30, the male death rate was rising, and the association between carcinogens excreted in the urine in dye-workers was well established. There was, however, no difference between the tumours occurring in dye workers and those in "normal" people. The symptomatology was well known, but the 90% incidence of haematuria could not be over-emphasized. Essential investigations in the clinical assessment of a case were (1) cystoscopy, (2) biopsy, the theoretical dangers of which were outweighed by the importance of the histological information produced (provided a decent-sized bit was removed), (3) bimanual examination under full relaxation anaesthesia, and (4) intravenous urography. The sum of the information revealed by these four simple tests determined the choice of treatment.

Treatment was discussed by Mr. D. M. WALLACE (London). His first point was the importance of the degree of infiltration of the tumour, judged on examination under anaesthesia and from the histological report. Mucosal (non-infiltrating) tumours were best treated by endoscopic resection or by diathermy. The "casual buzz at the end of an operating list" was deplored: it might be necessary to spend an hour or more on the job to do it properly. The 5-year survivals were 60–75%. The treatment of infiltrating tumours depended on the site: the rarely found tumour of the vault was amenable to wide excision, while the commoner tumours of the base were treated by interstitial radioactive tantalum-wire implant after removal of the bulk of the tumour with diathermy. The 3-year survivals of 145 implants were 91; the 5-year survivals of 74 implants were 43. Fixed tumours should be treated by high-voltage (preferably super-voltage) *x*-ray therapy. This might be followed by total cystectomy in certain cases, for, whereas surgery could safely follow radiotherapy, there was little to be said for the opposite way round. Treatment in this advanced group was often only palliative and long survivals were not to be expected. Persistent haemorrhage following radiotherapy might be due to hyalinization of the arteriolar walls, and for this cystectomy or ureteric transplantation might be needed.

Mr. R. MORRISON (London) described his experience of super-voltage therapy, mostly with an 8 MeV linear accelerator which has been in use since 1954. In addition to the whole bladder, the perivesical tissues and the regional pelvic lymph-node areas were irradiated. The treatment lasted four or five weeks and haematuria was usually controlled within two weeks. Dysuria and frequency might persist for six weeks or more after the end of treatment. Although only advanced disease had been treated in this fashion the results had been encouraging. About 30% of tumours had completely regressed and in a further 15% improvement

was observed. Five-year survival figures were not yet available, but in view of the fact that bladder cancer was a rapidly killing disease the 3-year figure of 21% in such an advanced group could be considered not too depressing.

SECTION OF OBSTETRICS AND GYNAECOLOGY

Tuesday, June 21

Sex Determination

With the president of the Section of Obstetrics and Gynaecology, Mr. H. L. SHEPHERD (Bristol), in the chair, Dr. J. A. FRASER ROBERTS (London) gave the opening paper in a discussion on sex determination. In the human, he said, the determination of sex was primarily genetic, but faults in the "switch-mechanism" could cause various intersex states. In particular, non-disjunction of the sex chromosomes at reduction division in either parent could produce instead of the normal male (*xy*) or female (*xx*) such syndromes as Klinefelter's (*xxy*) or Turner's (*xo*); non-disjunction in the mother alone could result in the super- or meta-female (*xxx*). The causes of non-disjunction were unknown, but parental age, genetic tendency, environment, and radiation were likely factors. Another form of non-disjunction, perhaps at the time of the first cleavage division, resulted in a mosaic pattern of sex chromosomes, the general incidence of which was unknown as yet. It was the *y* chromosome which in the human was strongly sex-determining, and *x* had to be fully and doubly present and with no *y* opposition for full female development to occur.

Other forms of intersex, continued Dr. Fraser Roberts, such as testicular feminization and adrenal virilization, might also be genetic in origin, with a sex-linked or sex-limited gene operative in the former and a recessive gene in the latter. Finally, he deplored the use of terms such as genetic sex or nuclear sex, for the decision as to the sex of an individual must be made on the final product as a whole, the picture of which was largely coloured by the early upbringing.

Diagnosis of Sex

Professor W. M. DAVIDSON (London) traced the history of the diagnosis of nuclear sex by skin biopsy, blood film, and buccal smear. The last two should be routine investigations in any case of doubtful sex. Originally it had been thought that the chromatin-positive nodule or drumstick, typical of the female, marked the presence of two *x* chromosomes, but recent research had thrown some doubt on their close linkage. The discovery of the abnormal chromosomal patterns in Klinefelter's and Turner's syndromes had done much to explain the discrepancy between the gonadal structure and the nuclear sex in these conditions, but the picture was further complicated by some cases of the former syndrome showing a mosaic pattern. He himself had an impression that in this syndrome, even outside the field of sexual activity, there was a diminution of masculinity in temperament and traits. There was still no explanation of the true hermaphrodite with ovarian and testicular tissue in the same gonad. Finally, he felt strongly that in any individual case of intersex the decision as to the course of action to be followed must be taken as early as possible.

Intersex States

Dr. G. L. FOSS (Bristol) presented a working classification of intersex states together with illustrative slides. With all available methods of investigation it was possible to diagnose the various types early and so ensure appropriate upbringing. The intersex states fell into three groups. First were congenital conditions, which were in turn subdivided into three—chromosomal aberrations (e.g., Turner's syndrome), other genetic defects (e.g., testicular feminization), and embryonic virilization (e.g., in maternal arrhenoblastoma). Secondly, there were post-natal conditions including adrenogenital and Stein–Leventhal syndromes. And thirdly there were pseudo-sexes in which a normal male or female was given the appearance of the opposite sex by the purposeful administration of massive doses of hormones combined with plastic surgery. In conclusion, Dr. Foss drew attention to routine nuclear sexing of the newborn as a simple screening test to detect degrees of intersex not obvious on external inspection. This would make possible the early study of these babies, facilitate treatment, and determine appropriate upbringing.

In the subsequent lively discussion, Mr. J. MACPHERSON (Torquay) described the case of a middle-aged nurse found to be an example of testicular feminization and therefore entitled to the designation of man-midwife. Dr. A. P. NORMAN (London) as a paediatrician emphasized the importance of the early diagnosis of congenital adrenal virilism, because some of these babies had electrolyte imbalance, the effects of which might lead to a false diagnosis such as pyloric stenosis. Mr. S. BENDER (Chester) recounted two cases of gynaecomastia, one due to prolonged use of oestrogen ointment self-prescribed for pruritus ani, and the other to stilboestrol given for adolescent acne; while Mrs. CONSTANCE L. BEYNON (Brighton) had seen virilization follow the use of an androgen–oestrogen mixture for menopausal symptoms. Others who spoke from the floor were Mr. H. G. E. ARTHURE (London), Dr. G. HUME (London), Dr. J. E. GRAY (Newcastle upon Tyne), Mr. J. R. NICHOLSON-LAILEY (Taunton), Dr. G. F. SALTER (Melbourne), and Dr. ELSIE WARREN (Hammersmith).

Wednesday, June 22

Cervical Incompetence

Mr. F. W. ROQUES (London), a vice-president of the Section, occupied the chair when Mr. S. G. CLAYTON (London) discussed cervical incompetence as a cause of some cases of repeated abortion. Such incompetence was nearly always due either to obstetrical trauma or to gynaecological operation. The typical history was of repeated abortions, usually in the middle trimester, preceded by bulging of the membranes through the os but little pain or bleeding. Local examination and hysterography were other diagnostic aids, while during pregnancy repeated vaginal inspections might detect the dilatation of the cervix at an early and operable stage. For treatment he did not favour the Lash operation of longitudinal segmental resection of the cervical canal or the Shirodkar repair with fascia. He preferred the innocuous method of simple anchored sutures of tantalum wire encircling the cervix. Removal of these stitches about two weeks before term allowed normal delivery. The results of surgical repair of the incompetent cervix in 22 cases at Queen Charlotte's Hospital since 1954 confirmed that a 60–70% cure rate, in terms of maturity, could be expected. However, he deplored the use of the operation where previous abortions had been in the first trimester or where the diagnosis of cervical incompetence was not incontrovertible.

Habitual Abortion

Mr. S. BENDER (Chester) said that the picture of habitual abortion had been obscured by an unwarranted pessimism in prognosis and an uncontrolled empiricism in treatment. Provided that there was no basic constitutional disorder such as lowered renal efficiency, and no underlying local derangement such as congenital uterine abnormality, the outlook was more hopeful than earlier statistics had suggested. In the absence of general and local causes, the underlying fault might be genetic. Some of these women eventually produced an abnormal foetus, and, conversely, a high abortion rate had been noted in women who had delivered abnormal babies. Recently there had been an attempt to incriminate naturally occurring antibodies in the mother's blood as a cause of repeated abortion.

Where no other cause was found, continued Mr. Bender, a "hormonal imbalance" was commonly postulated, but the supportive evidence was far from conclusive. For treatment

progestogens as well as androgens were now under a cloud as possibly causing virilization of the foetus if female. Few gynaecologists had not tried increasing doses of stilboestrol in women who had previously had only abortions, but as good results had been obtained without as with the hormone. One came, perhaps reluctantly, to the conclusion that close psychological support of these women was at present our most valuable therapeutic weapon.

In the discussion on these two papers Dr. H. E. REISS (London) said that his investigations, which included hysterography of a foetus, led him to believe that incompetence of the cervix was congenital in origin in about one-quarter of the cases. Mr. J. R. NICHOLSON-LAILEY (Taunton) pleaded for careful repair of cervical tears and against under dilatation of the cervix at gynaecological operations. Dr. A. BARKER (Whitstable) thought that the cervix was still being damaged by the application of forceps before full dilatation. Dr. MERVIN GOODMAN (Liverpool), Dr. D. G. KIBBLEWHITE (Yeovil), Dr. D. A. GORDON (New Zealand), and Dr. M. ALLERHAND (Warrington) also contributed to the discussion.

Virus Diseases in Pregnancy

Dr. A. M. SUTHERLAND (Glasgow), another vice-president, took over the chair when Dr. D. MCKAY HART (Glasgow) read a paper on virus diseases in pregnancy. He traced how the impact of different virus diseases on pregnancy had been studied after Gregg had described the rubella syndrome in 1941. The time of maternal infection with rubella was linked with specific abnormalities: at about 6 weeks infection produced cataract and cardiac lesions, and at 8 to 10 weeks deafness. The foetal risk had at first been exaggerated, and was now thought to be less than 20%. Smallpox was rare in Britain, but the maternal mortality was high, and abortion, prematurity, and stillbirth were very common. The virus of rubella, or smallpox, might affect the foetus even though the mother had previously had the disease. He therefore saw no point in encouraging young girls to contract rubella. In maternal chickenpox, mumps, and measles congenital deformity was not a significant risk. Nor was it in poliomyelitis, but the pregnant woman had an increased susceptibility to this disease, especially in the last trimester, when the mortality was almost 50%. Termination of pregnancy did not improve the prognosis for the mother. In general, he summarized, it should be remembered that in less than 1% of congenital abnormalities was there a history of any febrile illness in the mother during the first three months of pregnancy.

In answer to questions from Dr. D. G. KIBBLEWHITE (Yeovil), Dr. A. S. VALENTINE (Nottingham), Mr. M. J. HISHON (Australia), Dr. DOROTHY SANDERSON (Coventry), Dr. J. E. GRAY (Newcastle upon Tyne), and Professor G. G. LENNON (Bristol), Dr. HART said that gamma globulin was of very doubtful prophylactic value. He did not favour the termination of pregnancy for maternal rubella unless his psychiatric colleague advised him to do so because the patient had developed a gross mental reaction to the possibility of bearing an abnormal child.

Low Forceps in Domiciliary Midwifery

Mr. A. B. CONCANON (Plymouth), the third vice-president of the Section, took over the chair when Professor G. G. LENNON (Bristol) showed a film illustrating low-forceps delivery in domiciliary practice. He believed that only this type of forceps extraction should be carried out at home. For this operation it was unnecessary to anaesthetize the internal pudendal nerves at the level of the ischial spines. He injected the nerves as they entered the vulva from Alcock's canal at the anterior aspect of the ischial tuberosities. This was combined with local infiltration of the perineum and colpoperineal angle, and the woman might continue to use her gas-and-air or "trilene" machine if necessary. About 30 ml. of 0.5% lignocaine without adrenaline or "hyalase" usually sufficed. If the head was really low, it did not matter whether the occiput was anterior or posterior, for it could be delivered by Wrigley's forceps with an episiotomy.

Professor Lennon's excellent film and accompanying remarks evoked a lively discussion to which general practitioners and specialists alike contributed. Dr. D. A. GORDON (New Zealand), Dr. W. W. FULTON (Glasgow), Dr. LLOYD (Birmingham), Mr. F. W. ROQUES (London), Dr. J. G. R. CLARKE (Luton), Dr. N. O. HUNTER (Torquay), Dr. J. A. A. L. WOODHEAD (Prestwich), Mr. J. MACPHERSON (Torquay), Dr. M. GOODMAN (Liverpool), and Dr. M. ALLERHAND (Warrington) all spoke from the floor.

SECTIONS OF CHEST DISEASES AND OCCUPATIONAL HEALTH

Tuesday, June 21

Chronic Pulmonary Disease and Its Assessment for Work

With the president, Dr. L. W. HALE (Redruth), in the chair, Dr. JOHN FRY (Beckenham) opened the discussion. Britain had the highest prevalence of chronic bronchitis in the world, and consequently the largest number of respiratory invalids. In men between 40 and 60 the prevalence rate was about 17% (i.e., there were about three million chronic bronchitics in the country). The family doctor played an important part in caring for these respiratory invalids because of his intimate knowledge of their family circle. In assessing the patient's fitness for a job certain factors such as the probable course of the disease, personal and family problems, and a knowledge of the work should be considered. The family doctor had to rely mainly on clinical methods for assessment of function, but could also use simple instruments such as the Wright peak-flow meter. He should have better contacts with industrial medical officers. He had to decide how much interference was justifiable because of the conflicting claims of health and earnings.

Dr. P. HUGH-JONES (London) stated that the primary function of the lung was to regulate the oxygen and carbon-dioxide content of the arterial blood. The two processes needed in man were ventilation of the alveoli, and gas exchange between alveoli and blood. Disturbance of the first process was more common. Tests of ventilatory efficiency included maximum breathing capacity, mechanics of breathing, and spirometry, which measured total lung capacity and residual air. Gas-exchange tests consisted of measurement of distribution of gas, balance between gas and blood in various parts of the lung (i.e., ventilation–perfusion ratios), and diffusing capacity. There were also subsidiary or screening tests such as arterial blood-gas analysis, air consumption, a standard exercise, arterial oxygen by oximetry, and comparison of one lung with the other by bronchospirometry. This last was likely to be replaced by the use of compounds such as radioactive oxygen, which could be inhaled; and the ventilation, blood flow, and mechanisms of all pulmonary segments could be measured without discomfort to the patient.

Dr. C. B. MCKERROW (Penarth) described two types of relatively simple lung-function tests which could be done in most clinics where time, skill, and money for more complicated tests might not be available. Simple tests could give information about whether disability was due to lung dysfunction and whether the patient was getting better or worse. The most useful ventilatory test was the forced expiratory volume (F.E.V.) measured by the simple spirometer and electric timer. The Wright peak-flow meter had the advantage of complete portability but the disadvantage of not being able to show how long the flow could be maintained. Disturbance of gas exchange could also occur, and this could be measured by a simple standardized step test described by Hugh-Jones and Lambert. This measured the "ventilatory cost" of exercise.

On the practical side Dr. A. A. WHITE (Bromsgrove) described an attempt at solving the medico-social problems

which arose in a single industry with a high incidence of pneumoconiosis in the South Wales mining valleys in the post-war era. Suitable employment for ex-miners disabled by pneumoconiosis was emphasized by the Grenfell Committee in 1945, and the Austin Motor Company set up a factory in South Wales, where at first toy motor-cars and later car components were made. The labour force consisted entirely of ex-miners with pneumoconiosis, cases with active tuberculosis being excluded. The project had been a success owing to the high degree of mechanization and to the provision of medical and nursing care at the factory itself. The men adapted themselves well, their absence rates compared favourably with industry as a whole, and the knowledge gained had influenced favourably the attitude of new employers towards this disabled group.

Dr. W. JEAFFRESON LLOYD (Birmingham) stated that, of the 24 million people employed in industry in Britain, the majority worked in small groups and did not have an industrial medical officer. An attempt had been made to discover the number of workers who had been treated for tuberculosis, and this was estimated at 8 per 1,000. The number of chronic bronchitics was much greater. There was great variation in industry with regard to taking back workers who had suffered from tuberculosis. They were not suitable for heavy industry and the sputum-positive cases remained a problem. However, attempts should be made to return them to their orginal work if possible, which in many cases might be lighter than was imagined.

Dr. T. MCS. WILSON (Manchester) did not think there were any reliable tests for the working capacity of an individual, but there was some value in the estimation of the partial pressure of oxygen in arterial blood (pO_2) in relation to exercise. Many tests were confounded by the determination of patients to return to work at whatever cost to their health. One difficulty in the return of the disabled to work was the problem of transport between work and home, and the only solution was to provide door-to-door transport. Hypoxic patients were particularly sensitive to dust, which increased the resistance to the passage of air through their bronchi more than normal. Hence the importance of dust control. The biggest problem was the control of acute respiratory infections, and for this immediate administration of an antibiotic by the patient himself was advised. The industrial health service should be expanded and the responsibility of the factory doctor should be only to the employee, whose welfare should be his sole consideration.

Farmer's Lung

Dr. C. J. FULLER (Exeter) opened the discussion with a description of the disease which had first been described by Campbell and Fawcett. The largest number of cases occurred in Wales and north-west and south-west England, where the rainfall was higher than in the east. Most cases occurred between October and March after a summer of heavy rain. The condition could be divided into three stages. The acute phase, which was brought on by exposure to a massive dose of mouldy hay and corn, produced an influenza-like illness without *x*-ray changes. In the subacute phase there were dyspnoea, pyrexia, cyanosis, basal fine crepitations, but little and temporary fine *x*-ray mottling. In the chronic phase, which occurred after repeated exposure, there was permanent lung damage with emphysema, pulmonary fibrosis, and bronchiectasis. The tuberculin test was temporarily negative in a large number of cases and there was also a rise in the gamma-globulin fraction. The disease was probably due to protein sensitivity due to some substance present in "dust" from mouldy hay or corn.

Dr. F. H. STAINES (Callington, Cornwall) described the postal survey he had undertaken on behalf of the College of General Practitioners in East Anglia, South-west of England, and Wales to contrast the case experience in districts of differing rainfall, altitude, and types of farming. Questionaries were sent to general practitioners and chest clinics. G.P.s notified 215 cases of farmer's lung and chest clinics 258 cases. It appeared that the case rate per 100,000 was 1.2 in East Anglia, 4.0 in South-west England, and 12.6 in Wales.

Dr. G. STEWART SMITH (Exeter) then described the histological appearances in two cases where lung biopsy had been performed. In the first, a man aged 27, after four weeks' exposure to mouldy hay, the lung surface showed nodules resembling miliary tuberculosis. There were large numbers of tuberculoid systems with occasional peripheral giant cells. Some symptoms showed central necrosis. Tests for *M. tuberculosis* were negative and the pattern was that of a sarcoid reaction. In the second case, a man of 55, one month after threshing mouldy corn, there were small round cells with lesser numbers of plasma cells. There were scattered giant cells of foreign-body type, showing clefts possibly from dissolved out cholesterol. Brownish dust material was present, though not in giant cells. There were frequent lipophages but no doubly refractile material. Tests for *M. tuberculosis* were negative; the condition represented a chronic peri-bronchiolar pneumonitis and could have been a reaction to dust. He stated that Seal and Sully had in addition described more chronic end-results with fibrosis and honeycomb and cystic changes. Zettergren had produced rather similar changes in rabbits by exposing them to hay dust with and without fungus.

Dr. G. F. TROBRIDGE (Bovey Tracey) explained that simple tests of pulmonary ventilation in farmer's lung did not reveal the changes to be expected in view of the asthma-like illness. In the patient with a recent first attack the vital capacity was only slightly reduced, the maximum voluntary ventilation was almost normal, and the F.E.V. was usually over 70%. Arterial oxygen and carbon dioxide were both low, while after breathing 100% oxygen for ten minutes the arterial oxygen saturation rose to 100%. These findings suggested that the essential disorder was a pulmonary-diffusion defect. In a series of cases these changes persisted for about six months, though clinical recovery often preceded physiological recovery. The severity of the physiological changes bore no relationship to the radiological abnormalities, and severe disability could be found with a normal chest radiograph. In those patients who had recurrent attacks increasing fibrosis influenced the physiological findings, so that ultimately the condition became one of pulmonary hypoventilation and the presence and absence of a diffusion defect could not be diagnosed by the above means.

In conclusion, Dr. Fuller said that treatment with steroids produced a dramatic improvement in some cases. He drew attention to the industrial implications; farmers might develop permanent lung damage, and farmer's lung should be recognized as a prescribed disease in order that patients might obtain financial benefit.

SECTION OF GENERAL PRACTICE

Tuesday, June 21

Have Health Centres Justified Themselves?

With the president, Brigadier H. L. GLYN HUGHES, in the chair, a stimulating discussion took place in a crowded hall on the subject "Have Health Centres Justified Themselves?"

Brigadier Glyn Hughes introduced the subject by pointing out that the original plans had been to help the family doctors to work better, both with local authorities and in their own field of general practice. These concepts had naturally applied to different areas and to different types of practice, and each one had its own problems and difficulties. He felt that it was a good thing that there had not been a rush into building multiple centres at the beginning of the Health Service, for the lessons of experience were only now being learnt.

Dr. J. SLUGLETT (Bristol), from the William Budd Health Centre, gave the conclusions he had drawn from a survey he had carried out of health centres in Britain. He sketched

the history, from the Dawson Committee's report in 1920 through the B.M.A. Committees' reports of 1936–8, the Medical Planning Commission of 1942, and the Cohen Committee report of 1954. All these committees recommended that preventive and therapeutic care should be carried out jointly and co-operatively, that where health centres were built the family doctors should practise from them alone and not from other branch surgeries as well, and that these health centres should be looked upon as experiments, and that we should learn from them as we went along.

Dr. Sluglett considered that health centres had justified themselves in so far as they had improved conditions and buildings for the patients and had improved standards of general practice by avoiding isolation and encouraging routine examinations and use of available ancillary aids. He pointed out the practical difficulties of introducing these centres in established communities, the tasks being much easier in new towns. Economically they could never be expected to pay for themselves, and no family doctor could afford to pay the economic rental required. They must be subsidized by some authority.

Mr. J. ORR (Stranraer) gave an account of his own health centre that was built in an isolated town of some 6,000 inhabitants in south-west Scotland. All the practising doctors were in the centre, and they had a general-practitioner hospital of 30 beds next door with consultant visiting staff, radiological and pathological services, and a wing set aside for local-authority use.

He felt that his centre was a success and that it had improved standards and brought the three services together.

All those who took part in the vigorous discussion were constructively critical of health centres, but none of them had ever worked in one.

Dr. D. L. CROMBIE (Birmingham) noted that it was difficult to compare the standards in health centres with those of general practice outside. Those that were good succeeded because the sets of circumstances were just right. He felt that in these centres general practitioners were being "expensively re-educated and reorientated." Whether this was really necessary or not was another matter.

Dr. R. C. R. GETHEN (Guildford) pointed out that it was quite impossible for these centres to be run economically by practitioners alone, and also that it was quite unfair that those subsidized in these centres should be working in competition with those outside. Dr. E. VON KUENSSBERG (Edinburgh) said that the same work of the same quality could be done far cheaper by family doctors working their own practices.

Dr. ANNIS GILLIE (London) made the pertinent point that these centres had been planned long before the introduction of the N.H.S., and now after 11 years things were quite different. She felt that the loan scheme developed after the Danckwerts report was the most promising arrangement.

Doctor–Patient Relationship

Dr. DAG KNUTSON (Sweden) and Dr. R. M. J. HARPER (Barnstaple) both said that the attitudes of the public and the individual patient were of the greatest importance, and that the relations between doctor and patient were the crux of good medicine.

Dr. LINDSEY W. BATTEN (London) considered the medical monopoly of the health centre in any area was against the concepts of democratic freedom. Dr. JOHN FRY (Beckenham) remarked that British general practice was, and always had been, an independent and aggressively individualistic branch of medicine, and that British family doctors would never support the idea of practice from multiple health centres up and down the country. As places of experiment they were useful in selected areas, but few worth-while studies had yet been published from them. As for comparing qualities of medical care inside and outside these centres, it was doubtful whether they were any better than the solid general practice practised by the average good family doctor in Great Britain.

Latent Disease in General Practice

Brigadier H. L. GLYN HUGHES (London) took the chair at a well-attended meeting on this important subject.

Anaemia and Heart Disease

Dr. D. G. FRENCH (Kidsgrove, Staffs) spoke on latent anaemia and latent heart disease. Anaemia was a common condition but one difficult to diagnose clinically. The only certain method of diagnosis was for the family doctor to carry out haemoglobin estimations himself, but this was obviously not a practical procedure, and, provided the doctor was alert and always thinking of the condition and able to use the local pathological facilities, few cases would be missed.

Anaemia was not of itself a complete diagnosis; the causes and types must always be determined before specific treatment was given. The two most common types in practice were iron-deficiency anaemias and pernicious anaemia. On no account should vitamin B_{12} or folic acid ever be used for a clinically diagnosed case of "anaemia" until the specific type had been determined. Iron could always be used as a first step.

In a study in his practice Dr. French had found that 11% of 500 patients, aged 50 and over, had haemoglobin levels below 85%. At the end of three years 81 of these patients had died, and 57 of these had had anaemia.

Most heart disease remained latent, and the family doctor had to keep alert and up to date by attending postgraduate courses if he was to be able to pick out the early case for specific treatment. Routine examination of the patient's cardiovascular system should be done whenever opportunity presented. Congenital acyanotic heart disease was an uncommon but important group, and every infant should have his or her heart auscultated during the first year of life. Whenever a murmur was heard it was best to obtain the opinion of a consultant to confirm the exact type, and to investigate the possibilities of surgical cure.

The course of mitral stenosis had been revolutionized by surgery, and all patients should be assessed for possible surgical treatment. The dangers of pulmonary oedema must be remembered, especially during pregnancy.

Hypertension could only be diagnosed if the blood-pressure was taken. Those with significantly raised blood-pressures should be reassessed every six months. If E.C.G.s were abnormal (Dr. French used one in his practice), then rest, lighter duties, digitalis, and diuretics were indicated.

Of 19 cases of coronary disease seen in one year, 5 died suddenly with no previous symptoms. Dr. French had carried out E.C.G. examinations on 200 men in the 38–45 age group who had attended for unrelated ailments, and a surprising number had abnormal readings.

Psychiatric Disorders

Dr. A. U. MACKINNON (Leeds) said that it was important to recognize concealed and disguised manifestations of psychiatric disorders at an early stage.

The frequency of diagnosis of psychiatric conditions varied much with the observer. Reports on their incidence in general practice had ranged from 7 to 70%. The diagnosis was essentially a subjective one, and was influenced by the doctor's own emotional state, whether he was tired, irritable, overworked, worried, or dissatisfied. In considering these conditions it had to be remembered that no fewer than two-thirds would improve whatever was done.

The doctor was often faced with the difficult task of elucidating various somatic symptoms for possible emotional causes. One had to be aware of being too psychiatrically minded, for many seriously ill patients with debilitating illnesses presented with emotional symptoms.

Apart from the depressions, psychoses were rare in general practice. Endogenous depression, according to Dr. MacKinnon, affected up to 3% of patients. Early diagnosis required great clinical awareness, especially in distinguishing women with depression who often passed under such labels as

"chronics," "hypochondriacs," and "psychosomatics." The patient with the so-called minor or trivial ailment was usually using this as a disguise for his emotional upset.

Undiscovered Diabetes

Dr. D. L. CROMBIE (Birmingham) spoke on pre-diabetes and undiscovered diabetes in the population. The former were not yet suffering from clinical diabetes, but had a strong predisposition towards it and would probably develop the florid condition as a result of one of the many unknown life stresses. It was largely with cases of undiagnosed diabetes that Dr. Crombie was concerned.

Detection surveys had been carried out in the past, but few had been completed on representative samples of the population. These surveys had suggested that for every known case of diabetes there was one other as yet undiagnosed—most of these were obese patients over 50 years of age. It was important to pick up these latent cases, because they could all be benefited by treatment.

The College of General Practitioners was conducting a large-scale survey of a representative sample of the Midland population to establish the incidence of clinical diabetes and the fate of those who had glycosuria without being diabetic. A follow-up of this latter group would show how many would become diabetics. If, as was likely, large numbers of new diabetic patients were to be diagnosed by intensive surveys, either the hospitals would have to prepare to cope with these patients or family doctors must treat them themselves.

Rheumatic Disorders

Dr. G. M. R. HOLLIDAY (Plymouth) talked about the early diagnosis of rheumatic disorders. Dealing principally with rheumatoid arthritis and gout (which he thought was common in his area), he discussed the historical aspects, the incidence, diagnosis, course, and management of these diseases. Among the many points he made were that gout was relatively common in post-menopausal women; that accurate diagnosis could now be made with the aid of ancillary investigations; that it was important to appreciate the latent and prodromal symptoms, since by early diagnosis complications, especially of the renal and cardiovascular systems, might be prevented.

SECTIONS OF OCCUPATIONAL HEALTH AND OF PUBLIC HEALTH AND SOCIAL MEDICINE

Tuesday, June 21

Hygienic Food-handling

Under the chairmanship of Dr. A. MEIKLEJOHN (Glasgow), president of the Section of Occupational Health, the panel discussion led by Dr. J. C. GRAHAM (London), Dr. E. D. IRVINE (Exeter), and Dr. G. N. M. WISHART (Southport) ranged over the control of raw materials, procedures in the catering and retail food trade, the selection and supervision of food-handling staff, and the all-important problem of education. Dr. GRAHAM stressed that food manufacturers insisted on very strict standards in their own interest, quite independent of any supervision by public-health departments: these included careful checking of raw materials—which often had to be stored for long periods before they were processed—and of containers, as well as the processes of manufacture. Considerations of economy and hygiene combined to exclude actual handling so far as possible. Dr. WISHART spoke of the important role played by public-health departments in the checking of bulk foods imported from overseas, such as dried egg and coconut products, which could carry pathogens of intestinal infections. Much progress had been made in the development of procedures to control deterioration and infestation in transit. Dr. IRVINE paid a special tribute to the advances in catering and food hygiene, especially in the larger firms, since the Food Hygiene Regulations (1955) had come into force; leeway had still to be made up, especially in small retail and catering establishments, which often did not possess structural facilities conducive to clean food-handling.

Dr. GRAHAM said that in large industrial units in the selection of staff preliminary health surveys by industrial nurses were invaluable. These consisted of a health history and a superficial examination to assess personal cleanliness and to recognize foci of superficial sepsis. In his firm all staff had to undergo mass *x*-ray examination, and bacteriological examination of faeces and blood serology were carried out when there was a history of diarrhoea. He considered literacy and good visual acuity important attributes in the food-handler. Dr. MARGARET E. THWAYTES (York) supported the selective health survey by industrial nurses—unclean clothing justified rejection of any applicant.

Regular Hand-washing

Dr. GRAHAM considered "habit training" by supervisory staff essential. During some procedures periodic hand-washing on the factory floor was carried out under supervision. Film strips were a useful teaching aid.

All speakers agreed that regular hand-washing was the basic requirement for good food hygiene. Automatic foam dispensers and continuous roller towels were hygienic, acceptable to staff, and economical in use. Dr. IRVINE told of a firm which had installed paper handkerchief dispensers in close proximity to wash-basins in the processing rooms and had forbidden the use of ordinary handkerchiefs. This helped to prevent staphylococcal food infections.

Both Dr. Irvine and Dr. WISHART paid a tribute to the school-meals service; with the help and guidance of the Ministry of Health good structural conditions existed almost everywhere, and the organizers tended to appreciate their responsibility to the community and the need for close and friendly co-operation with public-health departments rather more than, in general, the wholesale and retail trade did. More should be done in the schools to develop clean-food habits, and especially the routine of hand-washing after using the lavatory and before eating.

Dr. Wishart outlined a programme of food-hygiene education which his predecessor had introduced in 1950 in association with the local education authority and the St. John Ambulance Association; over 1,100 members of the public, including many engaged in the catering trade, had attended evening courses since then. Almost 800 of them had voluntarily taken an examination, and 69% of these had passed. Since 1953 the Southport Technical College had run each winter a 26-lecture course on "Advanced Food Hygiene." The interest these stimulated in the town had led to the formation of an active Food Hygiene Association.

Speakers agreed that the public were becoming increasingly aware of the need for hygienic food-handling in their own homes; improving housing standards and increasing prosperity, which allowed the installation of up-to-date equipment such as domestic refrigerators, had played an important part.

Dr. MEIKLEJOHN (Glasgow) posed the topical question of the safety of food consumed in seaside resorts. The panel agreed that thanks to the legal standards governing the manufacture of ice cream and to the safety of our water supplies, iced foods and drinks were nowadays usually safe, but that continued vigilance was essential. Dr. J. H. WILDMAN (Paignton) stressed the need to ensure quick consumption of crab meat, which had a high natural content of bacteria, which, though not normally considered pathogenic, could cause gastro-enteritis if the crab meat were stored too long.

In winding up the discussion, Dr. C. METCALFE BROWN (Manchester), the president of the Section of Public Health and Social Medicine, took up the problem of food-poisoning due to prepared meat, and related an incident in the school-meals service. Large quantities of tongue had been boiled 48 hours before consumption, and had been allowed to cool slowly in warm weather because the refrigeration plant had broken down; many cases of staphylococcal food-poisoning

had occurred because a member of the kitchen staff had had septic skin lesions. The disregard of several basic rules had caused this outbreak—namely, the avoidance of a long interval between the preparation and consumption of meat foods, the need for rapid cooling and refrigeration after preparation, the reporting of skin sepsis by all food-handlers, and the neglect of a careful hand-washing routine.

SECTION OF OPHTHALMOLOGY

Tuesday, June 21

SYMPOSIUM ON CATARACT SURGERY

Intracapsular v. Extracapsular Extraction

With the president, Professor G. I. SCOTT (Edinburgh) in the chair, Mr. L. P. JAMESON EVANS (Birmingham) opened the symposium with his paper on intracapsular *v.* extracapsular extraction, and pointed out at once that the title should be amended, substituting *and* for *v.*, as in the world to-day our only hope of salvation lay in co-existence. The conditions under which each method was to be preferred were discussed. Extracapsular extraction was advisable when there seemed to be a risk of haemorrhage or vitreous loss as in high myopia, in cases of hypermature cataract or in cases complicated by previous glaucoma surgery, or when zonular rigidity was evident. The question was in many ways a personal one, depending partly on one's training and partly on subsequent teaching and experience. The use of antibiotics and cortisone had reduced the incidence and consequences of post-operative iritis in extracapsular extraction, but at the same time the intracapsular operation had become much safer, and was the procedure to be preferred in uncomplicated cases.

A great advance was the introduction of general anaesthesia, and this had been used in all cases during the preceding three years with the exception of a few in which the patient's general condition made it inadvisable.

Post-operative difficulty in adaptation of vision was due to (1) the limitations of the post-operative spectacle lens and (2) the reorientation of space following the change of image size. The post-operative complications of extracapsular and intracapsular extraction were classified and discussed. In a group of 33 cases in which one eye had an intra- and the other an extracapsular extraction, the comparisons of the final visual results and of the post-operative complications were made, but this could never be quite fair because much was often learned from the first operation.

First-class general anaesthesia, corneo-scleral sutures, and zonulolysin had made intracapsular extraction of little greater risk to the patient, but had not altogether outweighed the advantages of the extracapsular operation.

Modern Techniques in Cataract Surgery

Mr. E. C. ZORAB (Southampton) approached the subject of appraisal of techniques by an analysis of a survey he had made by sending a questionary to 160 of his colleagues, of whom 150 had sent valid replies. These he classified under the headings of anaesthesia, fixation, exposure, section, wound sutures, iridectomy, zonulolysis, the method of extracting the lens, re-formation of the anterior chamber, and post-operative dressing. The majority of surgeons used local anaesthesia, lid sutures, and cataract knife for the incision, a peripheral iridectomy, intracapsular extraction, using forceps, and double padding post-operatively. There was less agreement about fixation of the globe, wound sutures, zonulolysis, and artificial methods of re-forming the anterior chamber.

Zonulolysis was certainly valuable in a proportion of cases, but the enzyme was not quite so innocuous as was at first thought, and complications which might be attributable to it were (1) oedema of the conjunctival flap, (2) aggravation of Fuchs's endothelial dystrophy, and (3) rupture of the vitreous face some days after the operation. The use of the enzyme in infants and children was associated with a high proportion of vitreous loss, and was probably an undesirable procedure. The problem of intraocular lenses was purposely avoided, as it was not relevant to the discussion.

Complications in Cataract Surgery

Professor G. I. SCOTT (Edinburgh) selected 725 cases for discussion and for the assessment of the incidence of the complications of intracapsular extraction, an operation first performed in this country in Edinburgh 35 years ago. The recognition of the type of case likely to present difficulties was discussed, and consideration of the measures which could be adopted to make the patient safer for surgery and surgery safer for the patient was given.

With regard to operative technique, there were clear indications for the performance of a complete iridectomy in certain cases, and particular attention was necessary to the measures which released muscular tension, lowered intraocular tension, and facilitated venous drainage. The ways of achieving these objectives included local measures, or the use of curare and general anaesthesia. A preliminary explanation to the patient was valuable when local anaesthesia was employed. The complications of cataract surgery were likely to be few if the requirements of premedication, operative technique, and post-operative management were fully met.

An active discussion followed the opening papers in which a number of speakers took part, and in which the methods of anaesthesia, the necessity for capsulotomy after extracapsular extraction, the use of sutures, and the benefit to the patient of improved techniques, were considered. Participants included Mr. J. MASTERTON THOMSON (Torquay), Mr. M. DYKES BOWER (Exeter), Mr. E. K. ROY THOMAS (Swansea), Mr. A. G. PALIN (Bristol), Mr. K. FAWSSETT (Newbury), Mr. P. J. M. KENT (Stoke-on-Trent), Mr. A. J. B. GOLDSMITH (London), Sir TUDOR THOMAS (Cardiff), Mr. O. GAYER MORGAN (London), Mr. P. R. GREEVES (Plymouth), Mr. N. CRIDLAND (Portsmouth), Mr. J. R. HUDSON (London), and Dr. W. N. ROLLASON (Aberdeen).

Ophthalmic Operations in the Aged

Mr. A. G. PALIN (Bristol) pointed out in his paper on ophthalmic operations in the aged that, although the proportion of people on the blind register to the total population had decreased between 100 years ago and 50 years ago, it was again increasing and represented 1:500 of the population. Just over half the blind registered were over 70 years of age, and many of these could have their vision restored by nothing more elaborate than a cataract operation.

The idea that the elderly "could not stand" an operation was becoming obsolete, and the discouragement that surgery would be disappointing "because the retina would not be any good" was unjustified, as not more than 6% of the elderly blind had significant macular degeneration.

A survey of large numbers of cases undertaken between the ages of 75 and 100 showed that age itself was no bar to a satisfactory result. Sympathetic understanding, and post-operative sedation and the prevention of post-operative confusion, together with the early prescription of temporary post-operative spectacles, all helped to produce a successful result in the elderly patient.

Secondary Carcinoma of Choroid

Mr. A. J. B. GOLDSMITH (London) began his paper by emphasizing the necessity for the appreciation of the good functional results which were often achieved by the treatment of secondary choroidal deposits by irradiation. He cited a case in which a patient with secondary deposits from a scirrhous carcinoma of the breast recovered a visual standard of 6/5 in each eye, and whose survival for a number of years underlined the importance of not assuming that secondary deposits in the choroid necessarily meant a bad prognosis with regard to life.

General treatment of the patient was accompained by radiotherapy for the ocular condition. The lenses were not

protected and 4,000 r was given in 20 treatments. The outcome in this and two other cases showed that (1) choroidal metastases were not necessarily definite evidence of widespread dissemination, (2) cataract did not inevitably follow irradiation in the dosage used, and (3) irradiation did not damage the retina.

The selective action of radiotherapy on the choroidal deposits without retinal damage made it the ideal method of treatment in such cases. The lessons to be learned from the outcome in the three cases quoted were (1) that all secondary deposits in the choroid were radio-sensitive, (2) that irradiation improved the vision or prevented its further deterioration in about 50% of cases, (3) that no pain in the eye occurred in any of the cases treated, (4) that choroidal deposits did not indicate early death of the patient, especially with hormone-sensitive tumours, and finally (5) that it was the duty of the surgeon to offer this form of treatment in the expectation that useful vision would be retained until death.

SECTION OF RHEUMATOLOGY

Tuesday, June 21

Clinical Problems of Rheumatic Pain

This symposium, which was held under the chairmanship of Dr. W. S. C. COPEMAN (London), was opened by Dr. P. S. DAVIS (London), who classified the syndromes in which muscular skeletal pains are attributed—often inaccurately—to "neuritis." He discussed the three common causes of this syndrome: (1) cervical nerve root pressure; (2) thoracic outlet syndrome; and (3) pain referred down the arm from soft-tissue lesions, the latter being distinguished clinically by the absence of objective signs. Virus radiculitis was yet another group. Finally Dr. Davis postulated a mixed syndrome in which a primary lesion of the shoulder-joint, causing pain in the arm, was succeeded by a dropped-shoulder syndrome due to muscular hypotonia. Dr. Davis concluded by discussing the syndrome of rheumatoid neuropathy, which appeared to be occurring more frequently than in the past. It might be associated, but not exclusively, with steroid therapy. He said that it resembled a diabetic neuropathy rather than that associated with polyarteritis nodosa.

Dr. F. DUDLEY HART (London) stressed that there were at least 77 recognized types of arthritis, and that a simple diagnosis of "rheumatism" bore little diagnostic or prognostic significance. Since pain was the common symptom in all these conditions, the specific characteristics of this pain were often invaluable in making a diagnosis. He then classified eight of the principal patterns of pain seen in this group of diseases, including (1) the fleeting pains usually associated with rheumatic fever, but also found in many other conditions; (2) the "agony" of gout; (3) the characteristic blend of pain, stiffness, and weakness seen in rheumatoid arthritis and its variants; (4) the stiff "buttock ache" of ankylosing spondylitis; (5) the dragging continuous pain of malignant disease; (6) the stinging, burning type of pain found in herpes zoster, confusing until the rash appeared; (7) the numbness, burning, and tingling of neuropathy; and (8) the special pattern of pain in generalized osteoarthritis. He also described the peculiar severity of the pain in Reiter's syndrome, which was associated with a characteristically depressed and guilty expression on the patient's face.

Dr. A. ST. J. DIXON (London) discussed three of the many metabolic diseases of bone which caused "rheumatic pains"—namely, osteoporosis (spontaneous and iatrogenic), osteomalacia, and fibrocystic disease of bone. He developed the theme, with several examples of how, when any of these conditions were superadded to an existing arthritis, very gross bone destruction was likely to take place. The four common clinical manifestations of these conditions were: (1) crush lesions of weight-bearing articular surfaces; (2) calcification of intra-articular structures, which might be associated with joint effusions; (3) osteoclastoma formation in the region of joints due to excessive osteoclastic activity; and (4) pathological fractures ranging between complete breaks and small cracks which might be barely visible on *x*-ray examination. He believed that these conditions might be responsible for a far higher proportion of hitherto undiagnosable rheumatic syndromes than was generally recognized.

Wednesday, June 22

Symposium on the Place of Steroids in Rheumatoid Arthritis

With Dr. K. N. LLOYD (Cardiff) in the chair, this symposium was opened by Dr. W. S. TEGNER (London), who stressed that at no time had steroids been claimed as a "cure" for rheumatoid arthritis, and that some of the apparent disillusionment which followed their introduction was based on a misconception about this. Since approximately 85% of all rheumatoid arthritics would either achieve prolonged remissions or at least remain self-supporting, it was only in the remaining 15% in whom crippledom was threatened that these drugs should normally be considered. He stressed that an acute onset did not necessarily carry a serious prognosis, but progressive deterioration associated with nodules and a positive Rose–Waaler test could be considered as a relative indication for steroids. Another group was patients already crippled who had not yet received steroids, and a more controversial group of patients was the breadwinners in families who were unable to continue working. Each case must be decided on an individual basis, however. He stressed the danger of being lulled into a sense of false security by what he described as the "cortisone honeymoon"—that is, the first few weeks during which steroids were administered.

Dr. O. A. SAVAGE (London), discussing the complications of steroid therapy, pointed out that figures collected from eight rheumatism centres indicated that the incidence of dyspepsia during steroid therapy was very high (32%). However, the incidence of true peptic ulceration was not greater than in the general population. When an ulcer occurred it was extremely likely to give rise to a gastric catastrophe. Dr. Savage postulated that steroids did not generally cause ulcers, but prevented gastric erosions caused by salicylates from healing, the evidence being that they did not occur when A.C.T.H. or steroids were administered parenterally. Neither did they often occur when steroids were given for diseases in which salicylates were not commonly used as associated therapy. If an ulcer occurred, the steroid must be withdrawn in most cases, but in six patients he had been able to maintain this form of therapy after an elective partial gastrectomy. Other complications discussed included hypertension (13.5%), which was seldom troublesome; infections (5.5%), which always responded to appropriate antibiotics; arteritis and peripheral neuritis (4), which seemed to be increasing; fractures and vertebral collapses (3%); and severe bruising (3%), which was becoming more of a problem in long-term cases, and was presumably due to atrophy of supporting perivascular collagen. Deaths attributable to steroids amounted to 4.5%. Dr. Savage then discussed the preparation of a patient for surgery while on steroid therapy. He also emphasized that each steroid had a critical dosage level which it was dangerous to exceed.

Exact Dosage

Dr. H. F. WEST (Sheffield) re-emphasized this last point, and said that the exact dosage used was always more important than which particular preparation was chosen. In his opinion corticotrophin remained the drug of choice in long-term steroid therapy. Apart from the absence of gastric complications one obtained a more prolonged and natural result, there was less purpura, and fewer menopausal symptoms. Ideally one needed laboratory control, but it was possible with experience to assess the dosage very accurately in the absence of this. However, the patient needed to be intelligent, co-operative, and sufficiently dexterous to manipulate a syringe. In Dr. West's experience patients began to adapt themselves to cortisone and hydrocortisone within two or three months, but with the delta compounds, though adaptation took place, it was slower, and some benefit remained after three or four years. He did not think that

the newer preparations had any significant advantage over prednisolone. There was a discrepancy between experimental and clinical experience in the dose ratios of cortisone and prednisolone. This could now be explained on the basis of some experimental work he had just completed indicating that above a certain level the proportion of prednisolone excreted in the urine altered, and with it the relative potency of the drug. In his opinion the maximum dose ranges of the available steroids were: prednisolone 7½–10 mg. per day, triamcinolone 4–6 mg. per day, dexamethasone 1–1½ mg. per day. He pointed out that above this level one was taking over the function of the adrenal, and that this carried with it implications and responsibilities similar to those of any other "take-over operation."

ROYAL COLLEGE OF PHYSICIANS OF LONDON

FROM PALL MALL TO REGENT'S PARK

If all goes well, in about two years' time the Royal College of Physicians of London should be moving into its new home on the site of Someries House at the south-east corner of Regent's Park, between the Outer Circle and Albany Street The College has been at Pall Mall East—its fourth home—since 1825. The money for the new building has been found—the princely gift of £450,000 by the Isaac Wolfson Foundation was announced last September.[1] Any legal impediments to the College exercising its corporate functions from outside the City of Westminster[2] have been cleared away by the passing of the Royal College of Physicians of London Act on June 2.[3] The major planning permissions have been obtained. The architect's working plans are in hand. All that remains now is for the present occupiers of Someries House, the Ministry of Works, to leave.

Last week at the College Mr. DENYS LASDUN, F.R.I.B.A., architect of the new building, described its construction and demonstrated the model here illustrated (Figs. 1 and 3). He has had two overriding problems: his college must be "functional," tuned to its working needs, yet it must harmonize with its elegant Georgian surroundings. How he has resolved these at first sight conflicting requirements is told in his own words below. Certainly one factor in his success, as the President, Sir ROBERT PLATT, pointed out, has been the time he has spent in the present college, soaking up its atmosphere, observing its uses, and discussing future needs with the building committee. In every sense a modern building, the new college will also enshrine the past: as symbol of this the Censor's Room (Fig. 2), with the original panelling from the College's third home, in Warwick Lane, built after the Great Fire in 1666 had destroyed the house at Amen Corner,[4] is being transplanted bodily into the new building.

Architect's Description

Someries House was designed by Nash, but so many additions have since been made to it that the Gorell Committee did not think it worthy of preservation and recommended that it should be demolished. The new building will provide accommodation for the College Library of historical books, and will also include lecture halls, committee rooms, assembly rooms, dining rooms, common rooms for the use of Members and Fellows, and offices for secretarial staff. The building will be four stories high and is planned so that

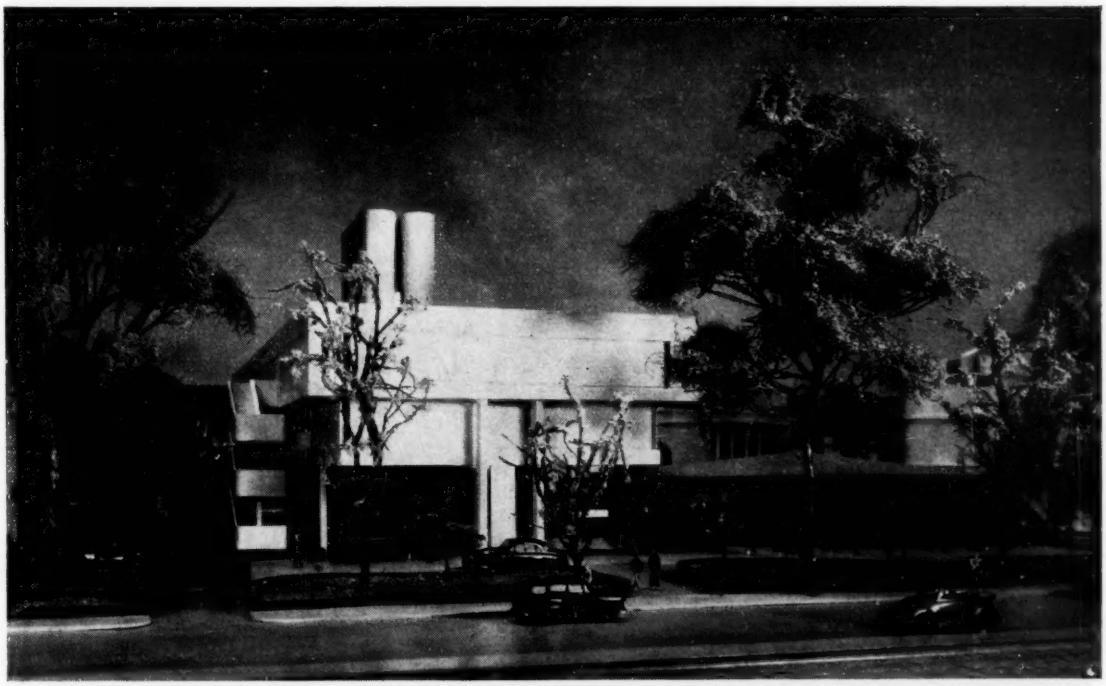


FIG. 1.—Model of the new building for the Royal College of Physicians of London, showing the main entrance as viewed from the Outer Circle. On the roof above the entrance can be seen the striking housing for the lift motors and ventilation plant. In the foreground the dark blue-grey wall and the copper roof of the main lecture hall are visible. (Figs. 1 and 3 are reproduced by permission of the *Architectural Review*.)

the principal rooms are grouped round a garden on the south side. A collegiate character has been aimed at, discreetly expressing the function of the building. The lift motor and ventilation plan room on the main roof acts as a visual weight, giving poise to the whole building. The Albany Street elevation is conceived as "street architecture." Great care has been taken to enhance the vista along St. Andrew's Place and to preserve its present atmosphere of a pleasant backwater. Care has also been taken to provide a sensitive junction with the fine Nash houses at the end of St. Andrew's Place and to maintain the scale of the adjoining buildings.

Ivory and Dark Blue

The building will have a reinforced concrete structure, the upper floors and columns of which will be faced with ivory-coloured vitreous mosaic. The lower floors, the main lecture hall, and the rear part of the building along Albany Street will be faced with dark-blue Baggeridge facing-bricks. The colours of the facing materials have been chosen to identify and harmonize the building with the cream-painted stucco and slate roofs of the Nash terraces.

The main entrance to the building will be at the west and facing Regent's Park. Cars will approach from St. Andrew's Place past the lecture hall, the façade of which will appear as a high raked garden wall leading in to the entrance. Parking space will be available on the site. The College Library is planned on the upper floors immediately over the main entrance and is reached by way of the main staircase which rises from a spacious hall in the centre of the building. Portraits from the College's collection will be displayed on the walls of the galleries surrounding the staircase. Bookcases round the walls of the Library will contain the important collection of historical books which was started by the College after the Great Fire of London. Meetings will be held in the Library and on these occasions the room will be able to accommodate 400 people.

Facing the Library at the head of the main staircase will be the Dining Room with accommodation for over 200 diners. The Dining Room may also be used for lectures and meetings, when 350 people could be accommodated. Separated from the Dining Room by a hydraulically operated movable partition and looking out over the garden will be the Long Room which will be used for receptions and committee meetings. The Dining Room will be served by a fully equipped kitchen. Both the Library and the Dining Room are two floors high with galleries at the upper level. To avoid deep overhangs within the rooms, these galleries have been projected outwards, giving the building its characteristic stepped section. This is further exploited in the central circulation space which grows upwards and outwards from the main staircase.

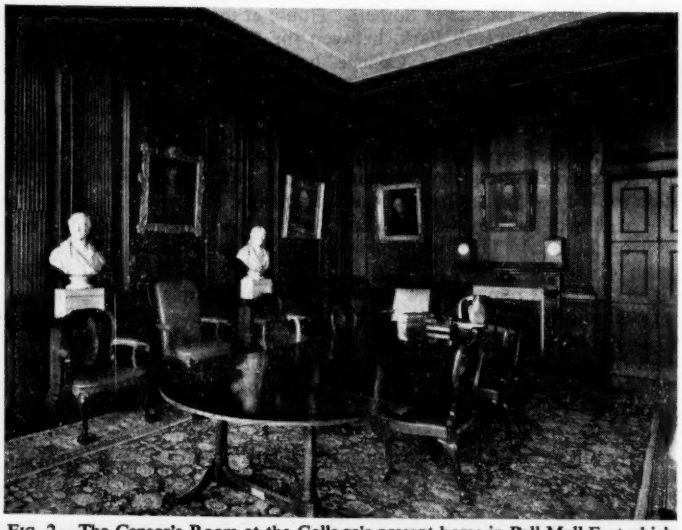


FIG. 2.—The Censor's Room at the College's present home in Pall Mall East which is being transplanted bodily into the new building. (Reproduced by permission of *Country Life*.)

FIG. 3.—Another view of the model, showing on the right St. Andrew's Place, which acts as the entrance to the garden court or precinct. The unobtrusiveness of the new design in its Nash setting is well shown in this picture.

Censor's Room and Lecture Halls

Opposite the foot of the main staircase, also overlooking the garden, will be the Censor's Room, which will be used by the college officers for meetings and examinations. This room will be a link with previous buildings occupied by the College, as it will be lined with the original Spanish oak panelling which was part of the building in Warwick Lane, designed for the College by Wren, and subsequently moved to the present college building, which was opened in 1825. The room is, in fact, symbolic of the long history of the College and has therefore been placed at the heart of the new building. Beyond the Censor's Room to the east are the principal officers' rooms and the main committee and council rooms, and beyond them again, in the part of the building fronting on to Albany Street, are the secretarial offices. The top floor of the building will be mainly occupied by library offices, bookstacks, and a reading-room.

Running south from the entrance foyer towards St. Andrew's Place is the main lecture hall, which will hold 300 people. The hall will have a stepped floor to give a clear view of the lecturer's demonstration table from all seats. It will be equipped for showing films and slides and there will be accommodation for up to five translators in sound-proof booths at the back of the hall. The roof of the lecture hall will be covered with copper sheet. There will be a smaller lecture-room holding approximately 50 people on the lower ground floor at garden level. Facing the garden at this level will be the staff dining-room and common rooms for Members and Fellows.

Cloakroom accommodation for up to 600 people will be provided in a lower hall below the main entrance foyer. There will be direct access between the main lecture hall and the cloakroom accommodation so that the lecture hall could be sub-let as a self-contained unit. Two passenger lifts will serve the main part of the building and there will be a third lift in the rear part of the building for use by the secretarial staff.

[1] *Brit. med J.*, 1959, **2**, 416 and 427. [2] Ibid., 1960, **1**, 123. [3] Ibid., 1960, **1**, 1822. [4] Ibid., 1959, **1**, 852.

Healthy and Wise.—The paragraphs below are taken from a leading article in the *Daily Mail* of June 25:

"There is a process known as auto-suggestion which medical men are familiar with. We are all prone to it. We have only to start reading a medical dictionary to feel that we are suffering from the symptoms of all the diseases in the book.

As one doctor put it, many patients leave the consulting-room feeling much sicker than when they came into it.

To-day we seem to be living permanently in the consulting-room. Medical advice is continuously directed at us from all sides—through television, radio, public pronouncements in the press, official or semi-official reports. The week of the B.M.A. conference is a particularly trying period.

Is it all good for us?

Luckily, perhaps, much of the advice is contradictory. The matter of the polluted beaches is an example. While some doctors say health is endangered, others (as reported in Parliament yesterday) conclude that the health risk can be ignored.

They can't both be right, so we can use common sense and keep clear of the plainly unwholesome areas (which do exist, as the *Daily Mail* investigation has discovered) until the local authorities concerned have done something about them.

Doctors themselves are a little bit worried that they might be turning the nation into a race of hypochondriacs.

A little caution would certainly be beneficial. We hear about too many wonder drugs which turn out not to be so wonderful after all. In America the situation is perhaps worse than here.

When a U.S. research team announced over-hastily that cancerous elements had been found in cranberries, sales of this fruit (which makes America's national sauce) dropped to zero. Vice-President Nixon was forced to eat a bowl in public in order to put the depressed cranberry growers on their feet again."

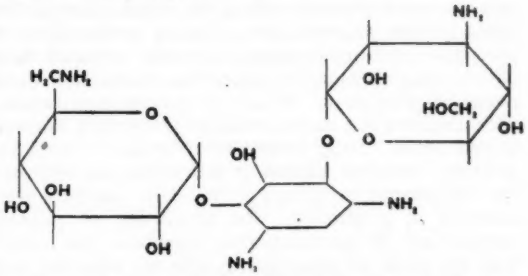
To-day's Drugs

With the help of expert contributors we publish below notes on a selection of drugs in current use.

Kanamycin

"Kannasyn" (Bayer Products).

Chemistry.—This antibiotic is derived from strains of *Streptomyces kanamyceticus*, and is chemically related to neomycin. It consists of two amino-sugars glycosidically linked to deoxystreptamine:



Pharmacology.—The *in vitro* antibacterial activity of kanamycin is identical with neomycin, and there is complete cross-resistance of organisms to neomycin and kanamycin. It is active against most strains of staphylococci so far isolated from clinical sources, and bacterial resistance can be induced among sensitive staphylococci in a slow stepwise fashion as is the case with penicillin.

The drug is only slightly absorbed from the gastro-intestinal tract, and has to be given parenterally for systemic infections. It is absorbed rapidly from intramuscular sites, and excreted by glomerular filtration, 50% to 80% of the dose being recovered in 24 hours.

Toxicity.—The important toxic effects are similar to those of neomycin, and, in particular, it can, like dihydrostreptomycin, cause an irreversible deafness. This is related to the level and duration of the serum concentration of kanamycin. Consequently, it should rarely be given to patients with impaired renal function, for in such individuals deafness may occur up to a week after withdrawal of the drug owing to persistent high levels in the serum. Proteinuria, casts, and haematuria may also be caused, but these changes are usually reversible unless there is pre-existing glomerular damage. There may be local irritation at injection sites.

All therapy should be stopped at the first evidence of tinnitus (which may precede deafness), deafness, proteinuria, oliguria, or a rising blood urea.

Therapy.—This drug should be reserved for serious systemic infections caused by staphylococci resistant to safer antibiotics, and for urinary-tract infections in which it is the only antibiotic to which the organism is sensitive. It is given by intramuscular injection in a dose of 1 g. daily in 2–4 divided doses, and, for children, not more than 15 mg./kg. body weight daily, in divided doses. The total dose given should not exceed 10 g., nor the course be longer than six days, with equivalent lower dosage in children. The patients should preferably be well hydrated, under 45 years of age, and with normal renal function.

Like neomycin, this drug can be used for the sterilization of the bowel, or for local application, but in Great Britain it is marketed only in a form suitable for parenteral administration.

Contraindications.—It must never be given to patients with poor renal function, a high blood urea, or dehydration, and should preferably not be given if other ototoxic drugs like streptomycin, dihydrostreptomycin, or neomycin have previously been given. It should never be used if the organism is sensitive to another and safer antibiotic.

N.H.S. Basic Price.—1-g. vial, 30s.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Iron Preparations for Anaemia

SIR,—With the exception of a few dissident voices it is now becoming generally recognized that some form of iron therapy should be given routinely to all pregnant women. It is useless to select those patients who are anaemic early in pregnancy for preferential treatment, because many patients with good initial haemoglobin levels become anaemic later. Many preparations of iron have been used; some are better tolerated than others; some are more expensive than others. Both these points, as well as the efficacy of various preparations, were discussed in a recent article by Dr. F. G. J. Hayhoe in your series "Drug Treatment of Disease" (April 16, p. 1195). Ferrous sulphate is both cheap and effective, but the general experience is that it is not very well tolerated in pregnancy. The proportion of patients complaining of gastro-intestinal symptoms has varied with the mode of presentation, with the observer, and with the dosage.

The problems of price and tolerance are now of major importance, particularly at the present moment when intramuscular preparations cannot be used. In an attempt to solve these problems an enteric-coated preparation of ferrous sulphate known as "toniron" was used at two local health authority antenatal clinics in Oxford. The tablets contain 5 gr. (0.32 g.) of ferrous sulphate, and the usual dose was three tablets a day. The preparation was very well tolerated and the price of the tablets was lower than that of any form of ferrous gluconate.

Haemoglobin readings (with the M.R.C. grey wedge photometer) were made at the first visit, and, as nearly as possible, at 38 weeks. The results, given in the Table, show an average rise of haemoglobin of about 9%. In assessing these results there has been no attempt to exclude those patients who were known, or suspected, to be failing to take their tablets regularly. This sort of exclusion is likely to be the result of careful inquiry about the patients whose haemoglobin levels are least satisfactory. A few patients (10 out of 105) were given ferrous gluconate for part of the time because they attributed minor gastro-intestinal upsets to toniron. The results therefore represent haemoglobin levels to be expected in average clinics containing the usual mixture of co-operative and uncooperative, truthful and untruthful, stupid and intelligent patients.

Haemoglobin Levels at First Attendance and at 38 Weeks

Clinic	No. of Pregnancies	At First Attendance		At 38 Weeks	
		Mean Week of Pregnancy and S.D.	Mean Hb % and S.D.	Mean Week of Pregnancy and S.D.	Mean Hb % and S.D.
A	51	18·2±6·0	88·5±8·7	37·5±1·2	97·1± 8·5
B	54	18·2±6·1	86·9±8·7	37·7±1·3	96·2±10·8

These figures make it clear that with intensive iron therapy it is possible to obtain a very high level of haemoglobin at term; in 75% of the pregnancies the level was 90% or more.

We wish to express our thanks to Medo-Chemicals Ltd. for a free supply of toniron for this trial.

—We are, etc.,

MARY FISHER.
ROSEMARY BIGGS.

Oxford.

Oral Diuretics in Pregnancy Toxaemia

SIR,—Drs. John D. Watt and Elliot E. Philipp (June 11, p. 1807) report five cases of intrauterine death following the use of chlorothiazide-type diuretics. In my opinion they wrongly assume that it is the diuretic which has caused the death. Lessening oedema, falling blood-pressure, and disappearing proteinuria are signs which presage foetal death, and are observable when the patient is having no hypotensive or diuretic. I agree with them that the use of these drugs does mask what is going on, and that is why I personally do not use them. Once a patient has been in bed sufficiently long for basic records to be obtained, then one should hope to see the blood pressure and the proteinuria gradually going up. If the conditions are stationary it means the foetus is not growing. If the patient is "getting better" she is doing so at the expense of the foetus, and amniotomy (which is the only treatment of "toxaemia") must be performed forthwith if the baby is to be saved. This accords with Sophian's concept of the aetiology of "toxaemia."—I am, etc.,

British Hospital for Mothers and Babies, Woolwich, London, S.E.18. C. K. VARTAN.

SIR,—We read with interest the letter on the use of oral diuretics in pregnancy toxaemia by Drs. John D. Watt and Elliot E. Philipp (June 11, p. 1807). We would draw their attention to an article recently published by us in this connexion.[1] In this article we drew attention to the problem of the suppression of maternal symptoms by chlorothiazide in pre-eclamptic toxaemia to which they refer.

We feel that it would be unfortunate if, as a result of their letter, the use of chlorothiazide in the management of pregnancy toxaemia was to be discontinued. There can be no doubt that, if the drug is used indiscriminately without proper observation of patients, cases of intrauterine death of the foetus will occur. We would suggest that the use of chlorothiazide in pre-eclamptic toxaemia be modified as follows:

1. Its use should be restricted to moderate and severe cases of pre-eclamptic toxaemia which do not respond to a period of complete bed-rest and the use of sedatives in hospital for a period of 48 to 72 hours. In our experience about 90% of cases of pre-eclamptic toxaemia admitted to hospital will require no additional treatment other than bed-rest and sedation. There would therefore seem to be no place for its use in out-patients in this condition.

2. The drug should not be used after the 38th week of pregnancy, when induction of labour will provide a more satisfactory result for both mother and foetus.

3. Patients under the influence of the drug must be kept under day-to-day surveillance in hospital. Under these conditions the maternal symptoms can largely be suppressed and attention for the most part directed to the welfare of the foetus. The problem of when to induce labour is difficult, and must be judged on the duration of the pregnancy and the rate of growth of the uterus. This problem exists in pre-eclamptic toxaemia, where the maternal symptoms are manifest, and, in our experience, the severity of the maternal symptoms does not always bear a relationship to foetal survival.

In our opinion, used as indicated above, chlorothiazide is of the greatest value in the management of pre-eclamptic toxaemia and has enabled us in many cases to allow a pregnancy to continue until a foetus

was mature enough to survive, although its rate of growth was considerably retarded by the toxaemic process.—We are, etc.,

ROBERT A. TENNENT.
DAVID W. LESLIE.

Maternity Hospital,
Bellshill.

REFERENCE

1 Tennent, R. A., and Leslie, D. W., *Scot. med. J.*, 1960, **5**, 113.

Thioridazine

SIR,—Your correspondent Dr. Douglas A. Kent (June 18, p. 1888) seems to have been singularly unfortunate in his finding that four out of his first six cases treated with thioridazine ("melleril") exhibited a pseudo-Parkinsonian tremor. He mentions other side-effects, such as light sensitization and periorbital oedema. The recording of side-effects such as these two latter is a question of degree, and in my experience it is quite common for patients receiving as little as 75 mg. daily to complain of nasal stuffiness which is probably due to oedema of the nasal mucous membrane. It is slight and seldom inconveniences the patient. It is, however, very surprising to learn that pseudo-Parkinsonian tremor occurred with such a low dose.

At this hospital some 400 patients have now received thioridazine in daily doses varying from 30 mg. to 1,200 mg. In only four cases was there clear evidence of the extra-pyramidal syndrome and in only one of these was tremor noted. I regard tremor as a late manifestation of drug-induced Parkinsonism and I believe it occurs only very rarely, after prolonged administration of at least 300 mg. daily of thioridazine. In passing, one should mention that "side-effects" are often observed during double-blind trials in the patients receiving the placebo. For example, in one series of cases three of our chronic patients on melleril developed a rash, but when a fourth case not on melleril developed a similar rash it was discovered that the rash was in all cases a staphylococcal one and nothing to do with the drug.

I feel that the impression given by Dr. Kent that all phenothiazine derivatives are "equipotent and equitoxic" should be questioned. Furthermore, that it is not only substitution in the 2-position of the phenothiazine nucleus that alters the pharmacological and clinical properties of the compound. Whilst it is true that substitution of, for example, $-CF_3$ for $-Cl$ in the 2-position produces trifluoperazine ("stelazine"), it must be remembered that this substance is potent in low doses and that it produces a high incidence of Parkinsonian side-effects. On the other hand, substitution in the 10-position only is carried out to produce perphenazine ("fentazin"), another derivative effective in low doses and producing a relatively high incidence of extra-pyramidal side-effects. Such are the idiosyncrasies of chemistry that substitution of the $-CH_2-CH(CH_3)N(C_2H_5)_2$ side chain in the 10-position gives us an anti-Parkinsonian agent ("ethopropazine"). It would therefore be idle to suppose that substitutions in the side chains of the phenothiazine nucleus do not result in radical alterations of clinical and pharmacological properties. Taeschler and Cerletti[1] have clearly demonstrated that thioridazine had different pharmacological properties to chlorpromazine.

Since 1952 the search has proceeded to find a major tranquillizer which is more effective in the treatment of schizophrenia than chlorpromazine and at the same time free from most of the side-effects associated with chlorpromazine. Most substitutions have resulted in compounds effective in much lower doses at the expense of an increase in their side-effects, especially extra-pyramidal ones. The writer and his colleagues have concentrated on the high-dosage phenothiazines and have spent five years in investigating the clinical properties of seven of these. In each case, I hasten to add, many more than six cases were investigated. Thioridazine appears to be the drug of choice, combining a freedom from side-reactions with clinical effectiveness in schizophrenia, a finding borne out by other investigators, notably Kinross-Wright.[2] Those of your readers who have carried out clinical investigations into new drugs on any scale will know that after a number of years spent in doing so one loses any emotional prejudices one may have in favour of any particular drug of choice. My own preference for thioridazine for the treatment of florid and overactive schizophrenics is based on extensive clinical experience, and I believe this drug should take its place, alongside other treatments, physical, psychological, and environmental, for the relief of mental illness.—I am, etc.,

R. A. SANDISON.

Powick Hospital,
Near Worcester.

REFERENCES

1 Taeschler, M., and Cerletti, A., *Schweiz. med. Wschr.*, 1958, **88**, 1216.
2 Kinross-Wright, J., *J. Amer. med. Ass.*, 1959, **170**, 1283.

Sciatic Syndrome

SIR,—Pain in the back and sciatica is a very frequent symptom in hospital out-patients, and the diagnosis of prolapsed disk is one that is often made. The treatment for this condition seems to be divided into four groups. (1) Placing the patient flat on his back in bed for a period of some three to four weeks. (2) The application of a belt or plaster. (3) Manipulative treatment with or without epidural injection. (4) Operative procedures.

The first two methods, while often successful, are very time-consuming, and we have treated a number of cases by the simpler method of epidural injection given under suxamethonium chloride anaesthesia. The epidural injection is given in the usual way for sciatica as already described by one of us,[1 2] and we now find that 50 ml. of 1% lignocaine with 25 mg. of hydrocortisone and 1,500 units of hyaluronidase added is a most suitable medium. The patient, who must of course have been carefully investigated before treatment, is placed on an operating table and anaesthesia is induced with thiopentone. The epidural injection is now given—the patient then placed on his back—and suxamethonium administered. This results in complete relaxation, and the weight of the patient, it would seem, is adequate to cause in many cases restoration to the disk that is prolapsed.

We have done some ten cases and the results have been successful, the pain and disability usually disappearing within 24 hours. No manipulation is attempted, other than traction to both legs, and a pillow is placed in the small of the back when the patient is returned to the ward. It is claimed that this method provides speedy relief in the cases in which it is used, and even in two cases where success was not complete relief was obtained. It is suggested as a method worth trying for this sometimes refractory condition.—We are, etc.,

GERALD SLOT.
R. A. HOGBIN.

Teddington, Hampton Wick, and
District Hospital,
Middlesex.

REFERENCES

1 Slot, G., *Practitioner*, 1933, **131**, 581.
2 —— *Med. Press*, 1938, **196**, 15.

Osteoarthritis of the Hip

SIR,—Recently in your journal there have been leaders, articles, and letters on osteoarthritis of the hip joint and congenital dislocation of the hip joint. There has been much discussion on the early diagnosis of C.D.H., but nothing about the early diagnosis of osteoarthritis. This is regrettable, as so much can be done in the early stages of the disease to retard its progress.

It is not generally realized that the radiograph of an early osteoarthritic joint shows no abnormality. Therefore the diagnosis of the early stages of the condition is made purely on clinical examination. The patient usually consults the general practitioner with aching and pains in the tissues around a joint with some joint stiffness. On examination it is often found that the range of movement of the underlying joint is restricted in one or more directions. This is particularly so in the case of the hip joint. If the hip and knee are flexed, the limb, instead of moving through the sagittal plane, moves so that the knee deviates and points to the outer side of the ipsilateral shoulder. In adopting the tailor or sartorial position, with the heel resting on the opposite patella, the knee and thigh remain elevated instead of rotating laterally. With the hip and knee flexed to a right angle internal rotation is limited. In the case of palpable joints, e.g., knee, carpo-metacarpal joint of the thumb, first metatarsophalangeal joint of the foot, the edges of the articular cartilage are felt to roll and are frequently tender to palpation, even though the radiograph is normal.

It is generally agreed that at any time symptoms may subside and the arthritic joint may become symptom-free, to remain so for an unspecified time. Progressive deterioration with exacerbations are, however, common. The success of any specific type of treatment will therefore depend to a certain extent on what phase the osteoarthritic process is passing through, and how advanced it is. If the diagnosis is made early the patient can often be rendered symptom-free and remain so for long periods by following a simple regime. Even in advanced cases it is often worth trying the effect of a short period of conservative treatment, or of combining it with minor operative procedures, before major surgery is considered.

In a weight-bearing joint there are several factors which can disturb the balanced contraction of the surrounding muscles and therefore its stability. These factors include injury, anterior poliomyelitis, wasting of the thigh muscles after a lumbar disk episode, congenital dislocation of the hip, or abnormalities in the bones forming the joints. Mechanically unstable joints in time usually become osteoarthritic.

There are two axioms which must be obeyed in order to achieve increased muscle power in an osteoarthritic joint: (1) Resting the joint from strain. In the case of the hip, knee, or ankle joints, this can be done by means of sticks, crutches, or callipers. (2) Exercises without straining the muscles or joints, performed preferably on a bed, in slings, or in a swimming-pool. There may come a time when operation becomes inevitable, but, as Mr. J. Charnley points out (March 19, p. 821), in the operative field there is a best type of operation for each case.

The patient with an early osteoarthritis of his hip, knee, or other joints must be made conscious of the fact that by a very active approach, which includes the right proportion of rest and exercise as well as other forms of conservative treatment, he may be kept symptom-free for years: but that if symptoms progress operative measures can give definite relief. Whatever happens, the patient must give up at least 30 minutes each day to treatment for his disability.—We are, etc.,

W. E. TUCKER.
R. P. GOULDEN.

London, W.1.

Care of the Old

SIR,—Two letters in your issue for May 21 deal with the important question of the relationship of the general practitioner to the local authority services (Dr. J. Maddison, p. 1565, and Dr. W. B. S. Crawford, p. 1568). Dr. Maddison accuses you of having a poor understanding of the functions and purposes of the local authority medical services, but himself exhibits a contempt for the work of the general practitioner in this sphere. Perhaps the patient and the profession would gain more from an attitude which looked forward to more active participation of the G.P. in the preventive services with closer links with the local authority auxiliary health workers.

In his work with certain categories of patients where the needs are often more social than medical, e.g., old people living alone and problem families, the general practitioner sees as his first responsibility the provision of adequate care. If this is not available through the local authority services (to be effective this means adequate help within 12–24 hours and often to cover week-ends and nights), the G.P. must get a hospital bed at the risk of being censured by the statisticians and the "surveyors," and irrespective of his willingness to treat the patient himself. If, as Dr. Maddison implies, there is no shortage of adequate help, perhaps this would be better distributed by better liaison between local authority and the G.P., but I believe lack of domiciliary help to be the main cause of admissions to the chronic sick wards. In the Birmingham area there is a shortage both of domestic help and trained personnel, both midwives and health visitors.

As Dr. Maddison describes, there are other categories of patients met with in general practice best dealt with outside the ordinary surgery hours. Most doctors cover this by having special sessions for their antenatal work, their immunizations, and the supervision of the post-natal mother and her infant. This work, too, is best done with the active co-operation of the local authority personnel, and in many areas, as in Birmingham, the local health authority makes its premises available or seconds either midwife or health visitor to the G.P. if he prefers to use his surgery premises. It would, in my view, be a retrograde step to replace this active co-operation with more local authority clinics; better to promote this co-operation so that the general practitioner takes his place at the head of a team responsible for the domiciliary care of the patient, both curative and preventive. Ideally this should be through group practice in a health centre, but much can be done now, with good will on all sides.

Dr. Maddison stresses the financial aspect of preventive work and rightly points out that the financial incentive for the G.P. is absent. Let us hope that this will be borne in mind by the working party in discussions with the Ministry. The sum paid by hospitals, local authorities, and miscellaneous other official sources for the year 1955–6, and deducted in determining the final settlement, was £2,918,377.[1] If the general practitioner is to extend his sphere of work to include more preventive work and more work on a part-time basis in hospital out-patient and casualty departments, this sum will increase to correspond with the increasing volume of work and responsibility. It also represents the value of work done by general practitioners for regional hospital boards and local authorities, and therefore should surely be removed from the calculations of the Central Pool.—I am, etc.,

M. BARROW.

Birmingham, 14.

REFERENCE

[1] *Report of Royal Commission on Doctors' and Dentists' Remuneration*, 1960, para. 318, Cmnd. 939. H.M.S.O., London.

Mental Health Tribunals

SIR,—The letter from Dr. F. E. Graham-Bonnalie (June 18, p. 1888) raises two points. Undoubtedly a considerable number of persons found themselves committed, in the past, to institutions for mental defectives in order to "solve" some family, social, or legal problems. My first experience of this was when I attended a court and was ushered into a room to sign certain papers. When I asked to see the patient, the police officer was both surprised and annoyed, as, I was informed, "this was an unusual request." My insistence upon seeing the girl and spending some considerable time with her was, I believe, the reason why this was also my last experience of being asked to attend to such matters. However, a large number of wrongfully detained persons have now been discharged, and, although one cannot say how many more such cases still remain, it is extremely doubtful if former practices will continue.

I anticipate that the work of the Mental Health Tribunals will be much more concerned with cases of psychoses, and this is a different matter. I agree with the view of the Minister that selected members of the profession should be appointed for this purpose, but it is arguable whether a hard-and-fast line should be drawn between recognized psychiatrists and others. There are many psychiatrists, undoubtedly competent in their special fields, who will be unsuitable for this particular task, and there are some doctors, practising in other fields, who happen to have the personality and some experience in this field to prove valuable members. Wherever possible, it seems to me, the psychiatrist on such a tribunal should not be engaged in any local or near-by mental hospital, for the tribunal has a legal function to perform. It is a sound tradition in this country that not only should justice be done but that it should seem to be done.—I am, etc.,

Reigate, Surrey. S. SHARMAN.

Petrol-vapour Poisoning

SIR,—The article by Dr. R. W. Ainsworth on petrol-vapour poisoning (May 21, p. 1547) recalled a similar case, in a 2-year-old boy, to which I was called a couple of years ago at Orewa, New Zealand.

He had seen his father siphoning petrol by mouth suction in a rubber tube from the car tank and he apparently had been trying to do the same when found in a very distressed condition by his mother. When seen he was semi-comatose and had signs of increasing shock. It was thought that he had swallowed the petrol, but two returns from the stomach-tube proved negative. His breath smelled strongly of petrol. He was dyspnoeic, slightly cyanosed, and had a fast thready pulse and lowered blood pressure. There were coarse crepitations and moist sounds all over the chest but most marked at the bases. While waiting for the ambulance he was held face down at an angle of 45°, whilst continuous light, fast tapping was applied to the chest using the ulnar border of the hand. Despite oxygen in the ambulance his condition was still critical on admission to hospital. By energetic treatment and despite nearly three days of anuria (which was thought to be caused more by shock than by the toxic effect on the kidney tubules of the small and variable amounts of cyclic hydrocarbons found in petrol) he was well enough to be discharged on the tenth day.

There is no doubt that he inhaled petrol in the liquid form, rather than just the vapour, and that this caused acute pulmonary oedema. Perhaps fortunately for him New Zealand petrol has a rating of approximately 70 octane.—I am, etc.,

Harrow. A. K. SAXTON.

Road Accidents

SIR,—Great stress nowadays is laid on the accident-rate of the alcoholic driver, and undoubtedly many fatal or serious accidents are caused by drunkenness or by hangover. But I believe that the bulk of accidents are the result of impatience and "showing off." Anyone who has succeeded in passing his or her driving test is entitled to obtain a high-powered car and proceed to find out what it "can do," often with sad results. It is not the elderly, deaf, or even poor-sighted driver, ambling, perhaps, rather far from his near side, who causes the accidents, but the younger who is determined to overtake no matter where it may be or what the conditions are.

So long as there is this thoughtlessness, jealousy, and lack of consideration on the part of pedestrians, cyclists, motor-cyclists, and car drivers the carnage will continue. Alcohol, apart from complete drunkenness, simply accentuates these inherent tendencies. I have no figures to prove it, but I believe that the daily rough-and-tumble, speeding to and from work, and even going shopping, causes more hospitalization than all the consumption of alcohol. I can think of no answer, but there must be one.—I am, etc.,

Ipswich. D. W. FRYER.

Oversea Career Appointments

SIR,—Apologizing for the inevitable delay in correspondence from overseas, may I add my support to the wisdom and insight expressed by Professor D. E. C. Mekie (April 23, p. 1274)? The time is overdue when a slip-stream from the "wind of change," which is blowing not only through Africa but through all emergent territories overseas as they advance to and gain internal self-government, might be directed towards stirring the dusty files which determine the conditions of service of officers in the medical branch of Her Majesty's Overseas Civil Service.

It is a matter of facing facts. We accepted appointments in the service of the Crown and have loyally worked in our allegiance to Crown, Secretary of State, and the local overseas governments to which we have been appointed. The work has provided us with the freedom and satisfaction of accepting the responsibilities, unique in these days at home, of being real doctors, calling on every inch of our training and medical curriculum to fulfil adequately the "do it yourself" call in every branch of medicine, surgery, and obstetrics. Standards are high; competent independence is a must; camaraderie is gratifying, and, in modesty, we think we do a man-sized job rather well. It is difficult to tame us again to a restricted field; we constitute a very specialized non-specialized service.

Why waste this training acquired by serving the millions overseas? They still need to be served, and we are best equipped to do so. However, come independence in these territories, and expatriate medical officers are offered either (*a*) a contract with the local indigenous government or (*b*) compensation for loss of office and a ticket home. The first does not often appeal, as new nationalistic governments are, perhaps unjustly, suspect as liable to alter conditions of service, pay, housing, passage arrangements, education allowances for children, leave entitlement, pensions, etc., and we dread becoming political pawns; as doctors we want simple but sound security and trust to get the best out of us. Our inbred loyalty too is, naturally, to our homeland and Queen. The second choice of lump-sum compensation commits us to abandoning the work we have lived for and learned throughout the years; it robs the local population of skilled, experienced, and trusted doctors; it requires the overseas doctor to seek for himself a job at home, in middle

life, and in most instances (there are exceptions) he will have to accept one in which he will be humdrum, hampered, and unhappy. I imagine that hospital gates are pretty well closed even for the surgical or medical specialist from overseas, and we are unaccustomed to "referring" cases.

The answer to this, I think, is the creation of an Overseas Branch of the U.K. Civil Service (Medical Division), for we are all, home or abroad, like it or not, civil servants. The U.K. Government should accept this responsibility, and not abandon or sacrifice the doctors they recruited for overseas service. The overseas territories need them and the trained doctors are there; but the doctors are being disbanded and the under-doctored millions overseas deserted. The creation of such a service would permit the doctors to continue their valuable work overseas, loyal to the Crown, with conditions of service assured, relaxed and contented in the knowledge that local political factions could rise and fall and yet they could remain disinterested and devoted. The question of payment would arise. Local overseas governments are normally poor; locally trained and locally recruited professional and technical staff know they cannot expect, nor do they require, expatriate rates of pay. Overseas governments could "hire" their doctors on contract from the U.K. pool by contributing their own local government rates, plus passages and assistance in children's education, whilst the U.K. Government could make up the deficit to the officer to U.K. rates. Indeed, it would be a whole-time salaried service, the officer being recruited, employed, and paid by the U.K. Government, but the latter recovering the contribution of local rate of pay, plus allowances, from the overseas government. Redundant doctors in the service could be absorbed into the U.K. service.

I realize these suggestions are akin to the Colonial Office's "Special List" proposals for West Africa or even to the creation of a Commonwealth Service, but I think something has to be done (*a*) to doctor the overseas territories, and (*b*) to stop the wastage and sacrifice of experienced and loyal H.M.O.C.S. medical officers.—I am, etc.,

Dar es Salaam, Tanganyika. R. MORTON MITCHELL.

Postgraduate Study for G.P.s

SIR,—In his letter (June 18, p. 1892) Dr. S. G. A. Bartlett welcomes the Nuffield Foundation's grant to enable general practitioners to study overseas, but criticizes the scheme on the grounds that the grant would have been better spent in allowing general practitioners to carry out postgraduate study in centres of their own choice in the British Isles.

This would be a valid criticism were it not for the fact that the College of General Practitioners is already able to offer fifteen fellowships each year to members of the College who wish to carry out special courses of study that cannot be carried out by means of standard postgraduate courses. Details of these awards can be obtained from the College office at 41, Cadogan Gardens, London, S.W.3, and I think that Dr. Bartlett would find that the awards that we can give for work in this country fulfil the requirements that he mentions in his letter.—I am, etc.,

Winchester. GEORGE SWIFT.

Pitfalls in Chemotherapy of Tuberculosis

SIR,—We were very interested to read the letter from Dr. R. Munro Ford (June 11, p. 1813) referring to our article (January 16, p. 161). In the first place we would point out that we were not so sweeping in our statements on "correct" and "faulty" regimes as Dr. Ford implies: these terms were used specifically in relation to the regimes used in those cases discussed in the article. Clearly this cannot exclude the acceptance of other regimes shown to be effective hereafter. Although Dr. Ford's regime of 2 g. streptomycin three times a week may be very effective, he produces no clinical or bacteriological evidence in his letter to support this, nor do we know of any published data proving that it is as effective clinically *and in preventing bacterial resistance* as the accepted M.R.C. regimes. Dr. Ford does not give details of the precise regimes of the drugs he uses with the streptomycin.

Our condemnation of streptomycin given three times a week was based upon the fact that, in the dosages so far reported, it does not dependably prevent resistance to another drug given daily. With our daily regime (streptomycin+isoniazid given under supervision) we have not yet encountered drug resistance. Even having regard to the 36–72-hour life cycle of *Mycobacterium tuberculosis* it remains to be proved that 2 g. streptomycin given three times a week is more effective than 1 g. daily: presumably reproduction is staggered! What is more, we feel there is significance in the 24-hour period for human beings—daily habits are easily made.

Apart from Dr. Ford's implication that present streptomycin regimes are ineffectual we can sympathize with his last paragraph. In this respect it would be very valuable if he would produce precise facts and figures relating to clinical results and bacteriological resistance in his series. If Dr. Ford's statements are confirmed his method could be an advance in therapy. Meanwhile we would reiterate the importance of never using regimes that have not shown themselves satisfactory in rigidly controlled trials.—We are, etc.,

GRAHAM POOLE.
PETER STRADLING.

Hammersmith Chest Clinic, Hammersmith Hospital, London, W.12.

Diabetes Insipidus after Tuberculous Meningitis

SIR,—In a careful study of the literature it appears that diabetes insipidus is a rare sequel to tuberculous meningitis. Presumably the case published by Lorber[1] and that published by Acheson and Smith[2] were white children, but every other case recorded appears to have occurred abroad, including two recently published cases in the *British Medical Journal* by Levin[3] and by Hay.[4] The following two case histories may then be of some interest in that they are apparently only the third and fourth cases occurring in this country. As the clinical courses of the two cases are very similar, only one is given in detail and the differences are mentioned later.

CASE 1

A 5½-years-old girl was admitted to Gateside Infectious Diseases Hospital, Greenock, on March 17, 1959, with a story of being listless, anorexic, and losing weight for a month previously. Two days before admission she became increasingly listless and failed to recognize her parents. She vomited once and was incontinent once. The drowsiness persisted and was the reason for admission, since clinical examination was entirely negative. Her previous medical history consisted merely of the usual childish illnesses—tonsillitis, whooping-cough, and measles. There was a family history of tuberculosis in that her mother and her younger sister had previously been treated in a sanatorium for pulmonary tuberculosis.

Examination on admission revealed a moderately ill child, rather underweight, pale and listless, but not irritable. Respiratory, cardiovascular, gastro-intestinal, and genito-urinary systems were all normal. Her pupils were equal and reacted to light and accommodation, but there was

marked photophobia. Nuchal rigidity was slight and Kernig's sign was negative. There was no muscle weakness and all reflexes were present and normal. Fundoscopic examination revealed no abnormality. Lumbar puncture produced an opalescent fluid with a high protein as shown by a strong positive Pandy's test, cell count was 320/c.mm., protein 300 mg./100 ml., sugar 18 mg./100 ml., and chlorides 630 mg./100 ml. Scanty acid/alcohol-fast bacilli were seen on direct microscopy. Her white blood-cell count was 18,400/c.mm. Intradermal Mantoux test 1/1,000 was strongly positive.

Antituberculous therapy was commenced on the day of admission. During the next three weeks her condition did not improve and on April 3 choroidal tubercles were seen in the left eye, and *x*-ray examination on March 30 showed miliary tuberculosis throughout both lung fields. In view of the lack of progress and in the absence of hydrocephalus steroid therapy was added to the chemotherapy. From this stage improvement was marked and she became afebrile on April 17.

On April 9 her cerebrospinal fluid was xanthochromic with the protein content almost 400 mg./100 ml., suggesting a block. There was, however, no papilloedema. Response to Queckenstedt's test was very slow, but the C.S.F. pressure was normal (70–120 ml. water on the manometer), and it was thought that the block was spinal.

On September 14 it was noticed that her fluid intake/output, which had been gradually increasing, amounted to some 7 pints (4 litres) a day, with a maximum urinary S.G. of 1010. Vasopressin tannate in oil, 0.5 ml., was exhibited subcutaneously. This resulted in only a slight fall in her fluid balance level. The effect of withholding fluid was tried and this resulted in the typical symptoms of dehydration, i.e., irritability, headache, and muscular pains. The vasopressin tannate in oil was continued for a month and the patient was then changed to vasopressin snuff thrice daily, which resulted in a considerable reduction in intake/output. The child, however, disliked the snuff and after six days refused to take it. It was therefore necessary to re-exhibit the vasopressin tannate subcutaneously, which, while reducing the level of the fluid balance, was not entirely satisfactory.

She was, however, discharged quite well on November 4. When seen as an out-patient on December 1 she was still passing large amounts of urine, but continued to have the vasopressin, which her father had been taught to administer. Reviewed on March 24, 1960, lumbar puncture showed a normal fluid, chest *x*-ray showed old miliary tuberculosis almost completely resolved, and the child had gained weight. Although she complained of occasional headaches, she had no sickness. She frequently wet her bed (2–3 times a week). She drinks large amounts of fluid and passes urine frequently, but still refuses to take vasopressin snuff, which makes her sick. Her appetite is poor and her bowels regular. She is back at school and leading a normal life. An attempt is now being made to stabilize her with varying amounts of vasopressin tannate in oil.

CASE 2

The second patient was admitted on July 5, 1953, a diagnosis of tuberculous meningitis was made, and treatment given successfully. She was discharged quite well in April, 1954. She was readmitted on October 25, 1954, with a story of polydipsia, polyuria, and enuresis. *X*-ray examination of the skull showed calcification in the region of the pituitary. The diagnosis of diabetes insipidus was confirmed by the response to vasopressin snuff.

The difference in these two cases was in the time lapse before the onset of the symptoms of diabetes insipidus. In the first case the symptoms gradually appeared from about 3–4 weeks after the diagnosis of tuberculous meningitis was made. In the second case there was a lapse of some 15 months. The second patient had radiographic calcification of her pituitary, whereas the first patient had not.

It is known that tuberculous meningitis exerts its most severe effects on the basal cisterns. It is interesting to note that in the first case the child was thought to have had a block, and it was more or less from this date that her fluid balance became disturbed and she exhibited all the symptoms of diabetes insipidus, probably due to mechanical damage to the pituitary by the tuberculous process itself without calcification, whereas the second case was probably caused by damage to the pituitary when calcification of the tuberculous exudate occurred.—I am, etc.,

Gateside Hospital, Greenock. JEROME P. WALL.

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3 Levin, A. R., *Brit. med. J.*, 1959, **2**, 1061.
4 Hay, D. R., ibid., 1960, **1**, 707.

Stein–Leventhal Syndrome

SIR,—The article by Mr. D. W. T. Roberts and Dr. Magnus Haines (June 4, p. 1709) on "Is there a Stein–Leventhal Syndrome?" raises points of interest. I would like to draw attention to the fact that the so-called Stein–Leventhal syndrome, described by them in 1935,[1] was actually described many years before, by Bartel and Herrmann in 1911,[2] in which amenorrhoea, menstrual irregularities, and sterility were stated as the clinical symptoms.

Rubin and Novak[3] stated that the French term *ovaires sclerokystiques* was the proper designation for this condition. The latter authors pointed out that in this condition one was dealing with the congenital type of polycystic ovaries, characterized by larger size, smooth or only slightly uneven surfaces, thick tunica albuginea, dense fibrous stroma, and a low total amount of follicles. The cortex is studded with small cystic follicles, many of them atretic. This congenital type of condition must be differentiated from another type of polycystic ovaries, which, owing to an abnormal activity of the hypophysis, have become polycystic. The stroma is normal, the tunica thin, and there is a normal content of the follicles. The increased size of these ovaries results only from their content of cystic follicles and recedes to normal when normal function is restored.—I am, etc.,

Royal Samaritan Hospital for Women, Glasgow, S.2. ALBERT SHARMAN.

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3 Rubin, I. C., and Novak, J., *Integrated Gynecology*, 1956, McGraw-Hill, New York.

Herpes Zoster with Chicken-pox

SIR,—Dr. D. Taylor-Robinson (June 4, p. 1713) describes a case of herpes zoster occurring in a patient with chicken-pox, and suggests that this is rare.

We had an outbreak of chicken-pox in the village here five years ago. A 70-years-old man developed typical chicken-pox on October 18, 1955, and two days later began to show fairly numerous lesions of herpes zoster on the left buttock and scrotum. He had been in previous good health, made a satisfactory recovery, and is still alive and well. There is some residual scarring of the affected area, but I doubt if the patient would agree to any attempt at emulating Dr. Taylor-Robinson's excellent photograph.—I am, etc.,

Alresford, Hants. JOHN S. HAPPEL.

Vesicles at Injection Sites

SIR,—Ten days after a 9-year-old boy had received a booster diphtheria injection in his left upper arm I was called to see him, as his mother thought he might have chicken-pox. He had a fairly heavy crop of small vesicles near the site of the injection and a few outlying spots on the neck. Thinking this must be a late allergic response, I gave the child some antihistamine, but within two more days he had developed a typical chicken-pox eruption over the rest of his body—the left upper arm being almost a confluent mass of spots.

I could find no reference in textbooks to an accentuated development of the chicken-pox rash at the site of the injection during the incubation period, and wondered if any others have noticed this. Would the mechanism be the same as that seen when paralysis develops in an arm injected during the incubation period of poliomyelitis ?—I am, etc.,

Ramsgate, Kent. W. G. BENSON.

Allergy to Tetanus Antitoxin

SIR,—In view of the report by Dr. I. B. Sneddon (May 14, p. 1468) we thought the following case might be of interest.

R. P., a laboratory technician, was working with tissue-culture apparatus and, in disconnecting a rubber tube, he accidentally splashed media on his face. Almost immediately he felt discomfort in the right eye, and 2–3 minutes later he developed acute chemosis of the conjunctiva of the right eye, the appearance being rather unusual, in that the involvement was predominantly of the bulbar conjunctiva and was limited by the limbus, with no involvement of the cornea. The palpebral conjunctiva was involved to a less extent, while there was almost no oedema of the lids. The accident had occurred at 5 p.m. and the eye had been washed out as soon as possible and adrenaline instilled into the conjunctival sac. "Anthisan" (mepyramine maleate) 100 mg. was then given orally. Symptoms gradually cleared over the next four hours and the only further treatment required was 50 mg. of anthisan at 10 p.m. By the following day the symptoms had disappeared and examination of the eye showed no abnormality.

As this appeared to be an acute allergy it was decided to skin-test for sensitivity to penicillin and horse serum, the media constituents most likely to be allergens. A small drop of penicillin solution 20,000 units/ml. and a similar drop of normal horse serum were placed on the forearm and scarification performed through the drop. Immediately irritation commenced at the serum site and within a minute a wheal appeared reaching a maximum diameter of three-quarters of an inch (2 cm.) with a surrounding flare of one and a half to two inches (4–5 cm.) diameter. This responded rapidly to antihistamine cream. The man had no past history of any form of allergy, although following bites by horse-flies a year ago he had developed oedema of the leg sufficiently severe to require bed rest. He had received T.A.B. vaccine and tetanus toxoid and had been immunized against diphtheria in 1942, but unless this immunization had been with T.A.F. he had no recollection of having had any horse serum.

It is possible that sensitization may have been due to handling horse serum in laboratory work, although there is no evidence for this. As a precaution he has been issued with a card stating that he is never to be given A.T.S. as he is sensitive to horse serum.—We are, etc.,

C. H. SMITH.
I. O. STEWART.

The Evans Biological Institute, Runcorn, Cheshire.

Clonal Selection Theory

SIR,—It is to your credit to have published the very provocative papers by Sir Macfarlane Burnet (October 10 and 17, 1959, pp. 645 and 720) on the somatic mutation theory of auto-immune diseases and the clonal selection theory of antibody production. This is a hypothesis which will be extraordinarily difficult to prove or disprove, but it is obviously very stimulating. It seems to me worth trying to extend the clonal selection theories to other diseases also.

One of the most obscure medical problems is why only one individual among many millions becomes hypersensitive to a usually unoffending allergen and develops asthma, or why only one patient among hundreds of thousands treated with the same drug undergoes a drug-induced agranulocytosis or thrombocytopenia. Such a discrepancy seems indicative of a random mechanism, and suggests a "somatic mutation" or "clonal selection theory" of asthma and drug agranulocytosis or thrombocytopenia. Because of the high number of replicating cells in the body undergoing mutation every day (10^6 according to Burnet), it is possible that a cell may occasionally acquire, after a mutation, the spontaneous ability to produce immune bodies or another specific response against a foreign substance. If this cell occasionally meets with this substance (inhalation of pollen, treatment with a drug, etc.) it will be selectively advantaged in the sense of Burnet and therefore generate a large clone genetically pre-adapted to produce the homologous immune or hyperergic body to such an extent to give clinical manifestations.

Only such a mechanism as random cellular mutation could justify the yet unexplained discrepancy between the number of exposed subjects and the number of patients who develop asthma or drug-induced agranulocytosis.—I am, etc.,

Department of Medical Pathology, University of Ferrara, Italy. ANGELO BASERGA.

Disseminated Histoplasmosis

SIR,—With reference to Dr. K. S. Rodan's letter (April 23, p. 1276) and the article of Drs. J. H. O. Earle, J. H. Highman, and Eunice Lockey (February 27, p. 607), I was interested to read Dr. Rodan's remark that in the case of histoplasmosis to which he refers necropsy revealed that both suprarenals were partially replaced by yellowish tumours which on histological examination showed masses of *Histoplasma*.

A case of generalized histoplasmosis in a European man who has been under my treatment since August, 1958, with amphotericin B ("fungizone") and corticosteroids, is under print for publishing in the *East African Medical Journal*. This patient showed, after an initial considerable improvement with the above treatment, a relapse presenting a typical clinical picture of Addison's disease. He again responded to treatment with amphotericin B and prednisone. At present he is again under the same treatment because of a further relapse of the disease. I have also noticed that in the case reported by Drs. Earle, Highman, and Lockey there was a temporary improvement under treatment with corticosteroids. I feel that it is important to draw attention to these facts about this treatment which, I feel, is worth trying in future cases.—I am, etc.,

Nairobi, Kenya. A. GELLERT.

Achromobacter anitratus

SIR,—In the summary of the article by Drs. D. L. Gardner, A. Pines, and Sheila M. Stewart entitled "Fulminating and Fatal Pneumonia and Septicaemia due to *Achromobacter anitratus*" (April 9, p. 1108) the statement is made, "Proof that this organism may behave as a pathogen has not previously been established."

I would therefore like to call to your attention a report,[1] entitled "Infections Due to Bacterium Anitratium," which presumably can be offered in refutation of the above statement, for it documents the case histories of three patients in whom "adequate evidence was present to establish a pathogenic role of [*sic*] Bacterium Anitratum." It should be pointed out that in this report, as it was originally published, the graphs for figures (cases) 1 and 2 should be interchanged. —I am, etc.,

Long Beach, California. GEORGE X. TRIMBLE.

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Unilateral Emphysema

SIR,—The objection of Mr. J. R. Belcher and his colleagues (May 28, p. 1654) to our use of the term "unilateral emphysema" (April 30, p. 1312) is apparently based on their own experience of patients with abnormal radiolucency of one lung. Their objection is relevant therefore only if we both happen to be dealing with the same disease entity and not just two groups of patients with a radiological sign in common. We did not claim, nor indeed do we believe, that emphysema is the cause of this *x*-ray anomaly in every case, as Belcher and his colleagues apparently do in regard to hypoplasia of the pulmonary artery. "We believe," they say, "that the radiological appearances in patients who present with abnormal unilateral radiolucency are due to hypoplasia of the whole or part of the pulmonary artery." I should like to make four comments about this statement.

1. Abnormal unilateral radiolucency may occur without significant reduction in the radiological size of the pulmonary artery, as in the case with large bullae compressing normal lung tissue which we quoted in our paper.

2. Abnormal unilateral radiolucency may be associated with functional and reversible changes in the pulmonary arterial tree (secondary to lung disease), without hypoplasia. This has been recorded in a patient with unilateral radiolucency by Swyer and James[1] and has been confirmed in animal experiments by Fouché and D'Silva.[2]

3. Some of the radiological appearances in our patients, such as the low flat diaphragm and the respiratory movements of the mediastinum, clearly cannot be directly attributed to hypoplasia of the pulmonary artery.

4. Their bronchospirometric finding of a reduction in oxygen uptake disproportionately greater than the impairment of ventilation certainly lends support to the view that there is hypoplasia of the pulmonary artery. But this is not so in every patient with increased unilateral radiolucency. In the three patients that we have now studied by this technique, in the patient reported by Dornhorst and others,[3] and in two of three patients described by Darke and others,[4] ventilation and oxygen uptake were about equally reduced.

We chose the title "emphysema" to describe our own particular group of patients because the clinical, *x*-ray, and physiological picture was indistinguishable (except in extent and degree) from that observed in patients in whom emphysema has been identified at necropsy. Direct pathological evidence of the nature of the lesion (or lesions) in patients with increased unilateral radiolucency is necessarily meagre, but in two cases, published by Belcher and Pattinson themselves,[5] the affected parts of the lung were reported as showing "emphysematous changes" and, in one case, these were "marked."—I am, etc.,

Liverpool Stanley Hospital, Liverpool, 5. COLIN OGILVIE.

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[5] Belcher, J. R., and Pattinson, J. N., *J. thorac Surg.*, 1957, **34**, 357.

Translating from Russian

SIR,—Professor D. H. Smyth's interesting article (May 21, p. 1561) will arouse the sympathy of the doctor who tries to translate Russian, and he raises some interesting points. To state that "information on the aspect of Russian verbs, though useful, is often not indispensable in technical translation" is to trail one's coat. A recent translation problem will illustrate this. The difference in aspect between доказывать and доказать (both listed in the dictionary as "to prove, to argue") is the difference between "to be in the act of proving" or "to be attempting to prove" (imperfective) and "to prove," implying completion (perfective). This is surely an important difference. Two of the examples he quotes of words missing from Jablonski and Levine could surely be "guessed without difficulty," неживой (non-living) не, not; живой living. Подрытый (undermined) is a literal translation под, under; рыть, to dig, to excavate (рытый passive past participle).

Professor Smyth's criticism that that dictionary falls by the system of listing is very real. Finally, I must endorse his suggestion that there is still room for the complete answer, set in clear type.—I am, etc.,

Manchester. W. R. LEE.

SIR,—With reference to Professor D. H. Smyth's article "Translating from Russian" (May 21, p. 1561), I strongly agree with him that a technical dictionary should be exhaustive and up-to-date as far as technical terms are concerned, and the omissions to which he refers in the newly published *Russian-English Medical Dictionary* by Jablonski and Levine are serious. All but one of these is included in the *Standard Russian-English Dictionary* (Lawrence and Wishart, 1943), which makes no claim to be a specialized medical work; it only needs a little imagination to find the appropriate translation in English technology. I have been able to translate many highly technical articles with the help of this book alone, and it has seldom let me down. Incidentally, it costs less than half the new dictionary. To translate any foreign work necessitates some general knowledge of the language, and one may have to hunt for the precise word (e.g., I found осумкование under сумка, a pouch or capsule; о-сумк-овать would naturally mean "to form a pouch or capsule," or encapsulation). Until the perfect technical dictionary is published, I should advise would-be translators to rely on a good general dictionary such as Lawrence and Wishart's edition of the official Russian-English Dictionary referred to above.—I am, etc.,

Ryde, I.O.W. L. FIRMAN-EDWARDS.

Rod and Serpent

SIR,—Major-General R. E. Barnsley's initial reaction (May 28, p. 1654) was the correct one; that is, when he dismissed as fanciful the suggestion that the staff of Asklepios was fitted with a mirror into which the serpent could spit venomously at its own image. I have recently had occasion to examine in the original, in photograph, or in facsimile some 36 different representations of Asklepios; these included statues, reliefs, paintings, and coins all dating from before the 4th century of this era. There was no indication in any of these that a mirror surmounted our legendary predecessor's staff.

The testimony of the classic authors denies that the serpents from the Epidaurian temple of Asklepios were venomous. Pausanias, in an account of his visit to this region in about 170, notes that "the serpents, including a peculiar kind of yellowish colour, are considered sacred to Asclepius and are tame with men."[1] Pliny informs us that "the Aesculapian snake was brought to Rome from Epidaurus and is commonly reared in private houses."[2] Aelian states that this serpent "is of a red colour, has sharp eyes and a wide mouth; its bite is not injurious but gentle. That, you see, is the reason why those who first made these discoveries consecrated it to the god who is the kindest to man and gave it the name of 'servant to Asclepius.'"[3]

More recently, in describing *Coluber flavescens (longissimus) s. aesculapii*, Gadow[4] notes that their distribution in south-eastern Europe favours the idea that these creatures were introduced by the Romans as inmates of the Aesculapian temples. The members of the sub-family *Colubrinae* to which the Asklepian serpent belongs are as a rule "intelligent and some of them become even affectionate." Gadow reports that the herpetologist Boulanger kept an Asklepian serpent for many years in a glass cage "where the snake entwined himself round the branches of a stick and allowed us to take him with the stick out of its socket and to inspect him."

Thus it is clear that the Asklepian serpent was chosen for its gentleness and not for any aggressive, venomous propensities. Eric Gill's emblem for the *British Medical Journal* is, I believe, a fair representation of the Asklepian attributes, whereas the mirror on the badge of the *Services de Santé des Armées de Terre, de Mer, et de l'Air* should be regarded merely as an amusing example of Gallic frivolity. The latter is, however, less reprehensible than the tendency among certain medical institutions to use as their emblem the caduceus of Hermes-Mercury, the messenger-boy of the Olympians and the Roman god of commerce. The winged staff entwined by a pair of coupling snakes is the one with which this god used to conduct the dead into the Underworld—with which, as Virgil says, "he calls pale ghosts from Orcus and sends others down to gloomy Tartarus"[5]; hence it is a more fitting symbol for an association of undertakers than for those devoted to the healing art.—I am, etc.,

Johns Hopkins Hospital,
Baltimore, U.S.A. HYMIE GORDON.

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5 Virgil, *Aeniad*, Book IV, 242. Loeb Classical Library; H. R. Fairclough, translator, 1929. Heinemann, London.

Diabetic Doctors

SIR,—I am collecting information on diabetes mellitus from the patients' point of view, and I should be most grateful if any diabetic doctor would kindly communicate with me.—I am, etc.,

The Memorial Hospital,
Midland Road,
Peterborough. G. F. WALKER.

Bell's Palsy

SIR,—The article on Bell's palsy by Mr. G. A. Dalton (June 11, p. 1765) appeared at the time when I had two cases of unusual interest. The actual disease was in both cases very mild, but occurred in two brothers with one day's interval between the onset of the two cases. The younger brother, who had his left side affected, was 10 years old, in my experience very early, although Mr. Dalton records one at the age of 5 years. The other brother, aged 21 years, had his right facial nerve affected. No reason has been found for the development of the disease in these two cases, but the simultaneous occurrence in two members of one family is in my experience unique.—I am, etc.,

London, N.W.6. J. A. GORDON.

Sir William Gowers

SIR,—I was much interested in reading Dr. Macdonald Critchley's account (June 18, p. 1829) of "The Beginnings of the National Hospital, Queen Square," and especially in his account of Sir William Gowers, who happened to be a personal friend of mine. One asset of Sir William's that was not mentioned was his outstanding skill in shorthand—and I have no doubt that this unusual accomplishment was a great help to him in his wonderful career.—I am, etc.,

Guildford. P. G. EASTON.

POINTS FROM LETTERS

Anal Dilatation for Respiratory Arrest

Lieutenant-Colonel W. D. KEYWORTH (Andover) writes: As long ago as 1912 I published an article in the *Indian Medical Gazette* on dilatation of the anus in the treatment of respiratory failure during chloroform anaesthesia, with suggestion for its use in cases of drowning. This article was well received in India. Chloroform is now hardly ever used in this country, but the spate of drowning cases and of persons suffocated in pits, pot-holes, gas-filled rooms, and collapsed buildings suggests to me that the value of this long-forgotten and long-discarded procedure be borne in mind by doctors and nurses engaged in rescue work. The only requirement was a little lubricant.

Osteoarthritis of the Hip

Dr. J. E. SWINBURNE-JONES (Blackpool) writes: I would strongly disagree with the advice given by Dr. E. H. Strange (May 28, p. 1662) that the use of a stick should be confined to the affected side. Having survived over three years the terrible onslaught of osteoarthritis of the right hip I have carefully studied which side to use an adjustable stick, and in my case it is most definitely the left side, which is the opposite side to the affected joint.

Side-effects of Phenelzine

Dr. G. J. BUDOW (Goodwood, South Africa) writes: To the list of side-effects given by Dr. J. Clarke (April 6, p. 1204) and Dr. H. Jacobs (May 21, p. 1570) I would like to add hypertension. I prescribed one tablet three times a day for a female patient suffering from neurasthenia with mild depression. The blood-pressure on first examination (as well as on earlier occasions) was 110/60. Two weeks later the reading was 140/80 and a further seven days later 160/100. At this stage the patient was complaining of a feeling of anxiety and palpitations. She was no longer tired on waking in the mornings.

Obituary

BERNARD ASCHNER, M.D.

Dr. Bernard Aschner, who was a gynaecologist in Vienna before emigrating to New York after Hitler's annexation of Austria, died in New York after a short illness on March 9. He was 77.

Dr. A. W. BAUER writes: Born in Vienna on January 22, 1883, Bernard Aschner graduated M.D. at the University of Vienna in 1907. After holding a lectureship at the Institute of Anatomy under Zuckerkandl, he joined the staff of the surgical university clinic under Eiselsberg, and obtained his first gynaecological training at the university clinic in Vienna under Schauta. During the first world war he served in the Austro-Hungarian Army and was in charge of an important surgical unit in Innsbruck. In 1918 he received the venia legendi for obstetrics and gynaecology at the University of Vienna. After Hitler annexed Austria he emigrated to New York, where he found a home from home and an enormous field of action. He was the head of the out-patient department for arthritis at the Stuyvesant Polyclinic and at the Lebanon Hospital. He published close on one hundred papers and a dozen books, which have been translated into most modern languages and have seen several editions.

Whilst serving at Eiselsberg's clinic in Vienna he discovered the oculo-cardiac reflex in 1908, called in Britain Aschner's phenomenon. In 1909 Aschner, using a new surgical technique, succeeded for the first time in removing the pituitary gland in young dogs. These dogs survived, and remained infantile dwarfs in contrast to the control dogs of the same litter. Thus Aschner demonstrated the hitherto unknown functions of the pituitary as an indispensable gland for growth and sexual development.

As a gynaecologist Aschner explored the relationship of the endocrine glands to the female genital organs. The result of his research on the influence of the pituitary upon mental capacity induced him to try somatic treatment of mental diseases, and he achieved surprising results in the treatment of melancholy and schizophrenia three years before Manfred Sakel published his results with insulin-shock treatment. His versatile mind had always been influenced by the old masters of medicine, and it will remain his uncontested merit that time and time again he called the attention of the contemporary medical world to the treasures of many therapeutic measures lying fallow in the works of these old masters. He maintained that by combination of earlier methods of treatment with modern diagnosis and technique many allegedly intractable diseases could be cured. At his Vienna out-patient clinic at the Allgemeines Krankenhaus, where I had the privilege of being his associate for many years, he applied the traditional therapeutic experiences with great success and taught that they should not be discarded because their rationale could not be explained. He translated and edited the entire works of Paracelsus, thus crowning his historical efforts.

Aschner was a great scholar and a striking individualist. His loss will be mourned by the great family of his patients in the old and new worlds. The memory of this great physician will be held in high esteem by all those who were familiar with his genius. He leaves a widow and a married daughter, to whom I extend my deep sympathy.

M. H. K. KANE, M.D., M.R.C.P.

Dr. M. H. K. Kane, formerly senior Government medical officer in Southern Rhodesia, died in King's College Hospital, London, on May 20. He was 67 years of age.

Michael Kane was born at Kingston Hill on April 18, 1893. From Rugby School he went on to study medicine at University College Hospital. During the first world war, as a second-year medical student, he served for a time as surgeon-probationer in the Navy, and then joined the Dublin Fusiliers, winning the M.C. He graduated M.B., B.S. in 1920, and in 1922 he joined the Southern Rhodesia Medical Service, remaining in that service until his retirement in 1949. Dr. Kane worked in many out-stations in Southern Rhodesia—Plumtree, Bindura, Gwanda, Rusapi, and Gwelo. In 1936 he took the M.R.C.P. and proceeded to the degree of M.D. For four years before retiring he was medical superintendent at Salisbury Hospital, Southern Rhodesia.

J. C. R. writes: I first met Mike Kane in 1947 when we both joined the D.P.M. course at the Maudsley Hospital. I was attracted at once by his patrician looks, his sardonic smile, and his very human laugh. These externals expressed the man himself; and the conversations which filled the intervals between our classes started a friendship which never wavered. He was a most interesting man. He had scientific observation and philosophical speculation joined in his thinking to an unusual degree, and his courage allowed him to adventure without any need for the approval of academic opinion. Unfortunately poor health prevented his continuing the course; but although his deep humanity was lost to clinical psychiatry he was able to rephrase in his writings the interplay between physical health and morality in the most interesting way. Although our circumstances kept us apart for most of the time, I have the memory of nearly 14 years of a most rewarding friendship.

C. H. STEINBACH, M.R.C.S., L.R.C.P.

Dr. C. H. Steinbach, who had practised in Knaresborough, Yorkshire, for 47 years, died at home on May 27, at the age of 78.

Charles Horace Steinbach was born on February 2, 1882, in Tasmania, came to this country at the age of 21, entered Guy's Hospital, and qualified in 1911. After holding the appointment of house-physician at the Evelina Children's Hospital he settled in Knaresborough in partnership with the late Dr. Bennett, and he remained in active practice there until a few months before his death, except for two years' service with the R.A.M.C. during the first world war.

Soon after his arrival in Knaresborough he was appointed medical officer to the County Institution (later Knaresborough Hospital), which he visited with enthusiasm and regularity until three years ago. His interest in the patients was considerable, and by observation and experience, and probably unrealized by himself, he became one of the first actively to practise the later established specialty of geriatrics.

He was by temperament ideal for the community in which he lived and worked. Slim and short, with an expression serious and even slightly severe, he would easily and quickly relax to manifest sympathy and humour. Unhurried in manner, he was methodical in all he did, and so considerable was his practice in the town and countryside that he had little time for interests other than his work. His week-end hobby was reading the journals, and he had the facility of quickly deciding and then applying which of the advances would be of help to his patients and to him.

Although never prominent in local affairs or medical activities he enjoyed his year of office in 1930 as president of the Harrogate Medical Society, and in 1934 as chairman of the Harrogate Division of the B.M.A. At meetings he spoke rarely, but when he did so, be the occasion formal or informal, he was indeed impressive, with a lucid and knowledgeable utterance which left a regret that he was not heard more often. His reward was not only the respect but the affection felt for him by his patients and his colleagues. The loss sustained by his family and by all who had been associated with him was shown by the large congregation at the service in the church of the parish in which he had lived.

He married Dr. Edith Goodison, of the Royal Free Hospital, in 1912; she died in 1921, and of the three daughters one is a squadron officer in Princess Mary's R.A.F. Nursing Service. In 1927 he married Miss Jean Read, who died in 1959, and of this marriage there is one son. To his daughters and son we extend our sympathy.—T. G. R.

J. K. MURRAY, M.B., Ch.B.

Dr. J. K. Murray died at St. Annes-on-Sea on May 16 after a short illness, at the age of 65 years.

John Kennedy Murray was born in Stockport, where his uncle, the late Dr. R. A. Murray, was a well-known figure. Educated at Fettes College and at Edinburgh University, he graduated M.B., Ch.B. in 1922. His studies were interrupted by the first world war, when he served as a probationary surgeon-lieutenant in destroyers from 1915 to 1918, but, in spite of this, he took an active interest in student affairs and was treasurer of the Union at the time that Lord Dunrossal was its president.

After qualifying, he was appointed to the post of house-surgeon at the Edinburgh Royal Infirmary, but the sea kept calling him back, and as soon as he was free to do so he was off once more, as a ship surgeon this time, and some years went by before he was ready to settle. From 1929 to 1941 he was engaged in general practice at Winchcombe, near Cheltenham, and in 1943 he came to St. Annes as a partner to the late Dr. R. Love Blair. He remained in active practice there until very shortly before his death.

Dr. Murray—Jock to his many friends—was conscientious and kind and completely unpretentious in everything he did. He was unflagging in his care of his patients and he would stay with those in trouble for hours if necessary until the crisis was past. He will be greatly missed at the St. Annes War Memorial Hospital, where he loved to work, and also in the homes of the many patients he looked after so well.

He married Miss Ann Farr, of Mold, North Wales, in 1930, and is survived by her and by two sisters and a brother.—D. K. L.

A friend writes: The death of Dr. J. K. Murray will be regretted by many to whom he was the ideal family doctor, and I should like to pay tribute to an old friend. He and I started off as medical students together and after service in the first world war resumed our studies to graduate together and become fellow residents in the Royal Infirmary, Edinburgh, in 1922, when "Wee Jock" was one of the most popular members of the mess. Some years ago our paths crossed again and I became one of his patients. His sound advice was characterized by cheerfulness, common sense, good nature, and humour. His great interest was in children, and his duties as medical officer to two children's homes gave him much pleasure. He loved children and had a wonderful way with them, and from experience in my own family I know how children liked him and looked forward to a visit from the doctor. The attendance at his memorial service reflected the esteem in which he was held.

B. T. SAUNDERS, M.B., Ch.B., D.P.H.

Dr. B. T. Saunders, who retired from general practice in Bolton four years ago, died in hospital at St. Albans on March 15. He was 69 years of age.

Benjamin Theodore Saunders was born on October 14, 1890. Educated at Aberdeen Grammar School and Aberdeen University, he graduated M.B., Ch.B. in 1913 and took the D.P.H. two years later. After completing a period as resident medical officer at the Aberdeen Fever Hospital he joined the Army, serving during the first world war in the Middle East and in France, and being mentioned in dispatches. On demobilization he became medical officer of health in Bagdad, returning to England in 1920 to enter general practice in Bolton.

W. J. C. writes: I first met Benjamin Theodore Saunders in 1907 at an R.A.M.C. camp on Deeside, when we were both medical students. He was a very fine rugger player, captaining the Aberdeen University team, and he took a very active interest in all sports. In 1920 he joined me in practice in Bolton, and from then on we had a long and happy association up to 1946, when I had to retire owing to ill-health. He was a most loyal colleague and friend, with a true sense of duty and a terrific capacity for hard work—and work is hard in a large industrial practice in Lancashire. He was greatly beloved by the patients and by all those who knew him intimately.

He did not take an active part in public affairs, but he was always interested in promoting anything that would help the welfare of the community. The second world war took its toll, but he continued in practice until four years ago, when he retired. His retirement, alas, was followed by a long series of illnesses. He will long be remembered, and we mourn his passing.

He leaves a widow, two sons, one of whom is in practice in Radlett, and a married daughter.

W. E. I. HEALY, M.B., Ch.B.

Dr. William Healy, who held an appointment at the Kilmarnock Infirmary before the onset of his last illness, died suddenly at his home in Glasgow on April 26. He was aged 43.

J. R. writes from New York: I learned to-day of the sudden and tragic death of my very dear friend and colleague Bill Healy, and I would like to express my appreciation of this very fine gentleman and physician. He was educated at St. Aloysius School and Glasgow University, and was one of the many young men who interrupted his university studies to serve as an executive officer in the Royal Navy during the second world war. The maturity and philosophy which he brought back with him to Gilmore Hill did much to enrich the undergraduate life of his many friends, and he carried this remarkable understanding of people into his postgraduate practice. His untimely demise at such an early age has denied him many of the honours afforded to his seniors, but to his many friends his warmth and understanding will be his perpetual memorial.

WINIFRED E. HADDEN, M.D., D.P.H.

Dr. Winifred Eileen Hadden, who practised in Portadown, Northern Ireland, died suddenly on May 4.

Winifred Eileen Hadden was born in 1894, the only daughter of the late Dr. W. E. Hadden, of Portadown. Graduating M.B., B.Ch. at Queen's University, Belfast, in 1920, she took the D.P.H. in 1922 and proceeded M.D. in 1935. After qualification she went into practice with her father. Dr. W. E. Hadden was a founder member of the local association of the Medical Women's Federation and an active member of the Co. Armagh welfare committee since its inception in 1947 and of the south-western special care management committee. In 1956 she was appointed to the Child Welfare Council of Northern Ireland. Her range of interests was wide, and she acted as honorary secretary of the committee on psychological and spiritual healing of the Methodist Church in Ireland since its formation.

Outside the practice of medicine she was interested in and supported the Portadown Musical Festival Association, of which she was honorary secretary for some years, and she sponsored and supported the Council of Social Services, giving much of her time to its many interests since its inception in the early 1940's, serving also on the executive committee of the Northern Ireland Council of Social Welfare. Another of her interests was the Portadown Soroptimists Club, which she helped to form and of which she was president for a term.

Leading a very active and useful life both in general medical practice and in social work, she was always keenly interested in every new development in medicine. She had a personal gift of being a helpful adviser, with a quick understanding of people's problems.

Since her father's retirement she worked in partnership with her youngest brother, Dr. R. E. Hadden, who survives her. Her two other brothers, both doctors, died a number of years ago.

J. G. McGREGOR, M.B., Ch.B., J.P.

Dr. J. G. McGregor, who was in practice for 42 years in Castletown, Caithness, died at Thurso on June 3. He was 77 years of age.

John Grant McGregor studied medicine at Aberdeen and graduated M.B., Ch.B., in 1906. After this he was for a time medical officer to Kingseat Mental Hospital. He then went to Singapore, where he was on the staff of the General Hospital for three years. Returning to Scotland, he practised for 18 months in Armadale, Sutherlandshire, and then moved to Castletown, where he remained until he retired. He was honorary secretary of the Caithness and Sutherland Division of the B.M.A. from 1941 to 1947. During this time he was also a representative on the Representative Body on five occasions. He gave much time and thought to Association work. At the beginning of the National Health Service he was elected chairman of the Caithness Local Medical Committee, having previously been chairman of the Medical Practitioners of Caithness Committee, of which body he was the founder.

W. I. A. F. writes: With the death of Dr. McGregor there has passed away another stalwart of that devoted band who made the Highlands and Islands Medical Service a credit to Scotland and the envy of many other countries. Of a somewhat reserved disposition, his work was characterized by a quiet efficiency. Widely read and with a diversity of interests, his wise judgment and sound counsel were welcomed by patients and colleagues alike. His advice, though never thrust on anyone, proved always worthy of the closest consideration. He was an ardent Freemason and attained high rank in the Masonic order. Golf and cricket were his chief pastimes and he was well above average in both, while local football owed much to his support and encouragement. His passing is greatly to be regretted, and our sympathy goes out to his widow and to his son, who is also a doctor.

G. S. DAVIDSON, M.B., Ch.B., F.R.C.S.Ed. F.R.C.O.G.

Dr. G. S. Davidson, formerly consultant obstetrician and gynaecologist to the North-East of Scotland Regional Hospital Board, died suddenly in a London nursing-home on June 4. He was 68 years of age.

George Stewart Davidson was born in Aberdeen in 1892 and received his early education first at Robert Gordon's College, Aberdeen, and later at Merchiston Castle School, Edinburgh. He graduated M.B., Ch.B. at Aberdeen University in 1916. In 1910 he had joined the R.A.M.C.(T.A.), and during the first world war he served as a captain in the R.A.M.C. from 1916 to 1919. He went to Salonika with the 43rd General Hospital, and served with the Serbian Army. Appointed to the Order of St. Sava and awarded the Serbian Silver Medal for distinguished service, he was twice mentioned in dispatches. On demobilization he returned to Aberdeen as house-surgeon under the late Sir Henry Gray, and house-physician at Aberdeen Infirmary.

Turning to gynaecology and obstetrics as the specialty of his choice, he worked under the late J. Haig Ferguson in Edinburgh Royal Infirmary. He also studied in Dublin, Liverpool, Manchester, Paris, and elsewhere, and took the Fellowship of the Royal College of Surgeons of Edinburgh. Returning to Aberdeen in 1923 he was appointed assistant obstetrician to the Aberdeen Maternity Hospital and surgical tutor to the Royal Infirmary. In 1930 he was appointed gynaecologist to the Royal Infirmary and subsequently lecturer in clinical obstetrics and gynaecology in the University. A Foundation Member of the Royal College of Obstetricians and Gynaecologists, he was promoted to the Fellowship in 1939. In that year he was vice-president of the Section of Obstetrics and Gynaecology at the Annual Meeting of the British Medical Association in Aberdeen.

Dr. Davidson married Dr. Elizabeth Logan, a medical graduate of Edinburgh. She survives him together with a son and three daughters, one of whom is also a medical graduate.

Sir DUGALD BAIRD and Dr. GEORGE P. MILNE write: George Stewart Davidson was the first obstetrician in the North-East who was also trained in operative gynaecology, and he acquired a very large private practice. In his earlier days in obstetrics he made contributions arising from his studies of oxygen therapy for the apnoeic infant, and he also wrote about puerperal fever and uterine displacements. George Davidson was rather retiring and shy in manner and did not take a very active part in committee work, but he was universally respected and liked and was affectionately known as "Jeff" to all his friends. In 1950 he retired from both hospital and private practice to take up residence in Jersey. Gardening was his hobby and his family his greatest interest.

G. H. CHEYNEY, M.R.C.S., L.R.C.P.

Dr. G. H. Cheyney died in a nursing-home at Reading on May 7 at the age of 80.

George Hammond Cheyney was born on January 3, 1880, and qualified from Guy's Hospital in 1905. For many years thereafter he was in general practice in Caversham and Reading. During the first world war he was medical officer at the war hospitals in Reading and Caversham, and during and after the second world war he served on Army medical boards. In the days of the Poor Law he was a district medical officer, and in the early years of National Health Insurance he was a member of the local panel committee. Until his retirement at the end of 1949 he was medical officer of Queen Anne's School, Caversham, and he was also a governor of the Reading Dispensary Trust, in the work of which he was particularly interested.

Dr. Cheyney is survived by his second wife, and by a son and daughter of his first marriage.

E. M. JONES, M.R.C.S., L.R.C.P., D.P.H.

Dr. E. M. Jones, medical superintendent of Ely Hospital, Cardiff, died at the hospital on June 13. He was 61 years of age.

Edmund Mervyn Jones received his early education at Howard Gardens Secondary School, Cardiff, and in 1917 entered the medical school at Cardiff for his preclinical studies. He went on to St. Bartholomew's Hospital, and after qualifying in 1922 was house-physician, house-surgeon, and senior resident medical officer at the Westminster Hospital. After these appointments he served the Cardiff City Council as district medical officer under the Board of Guardians, and while doing this work he gained the D.P.H. (Wales) in 1927. His work was in the thickly populated docks and industrial areas of Cardiff, and it brought him into contact with people who will always remember him for his great kindness and friendship.

In 1943 he was appointed medical superintendent of Ely Hospital, where he had the care of over 500 mental defective and senile cases. His relationships with the patients and the staff were always particularly happy, and he worked with a devotion which has seldom been surpassed. His sincerity and loyalty to those around him, especially his administrative staff, endeared him to them. He was a first-class chess player, but his greatest interest and hobby was the game of bowls. In this he excelled, winning the championship of Wales in 1953 and the pairs championship the previous year. His many friends, his patients, and his staff will mourn his loss as a loyal companion and a great gentleman. Our sympathy is extended to his widow—M. G. W.

Medical Notes in Parliament

SCOTTISH MENTAL HEALTH BILL

[FROM OUR PARLIAMENTARY CORRESPONDENT]

Before the Mental Health (Scotland) Bill completed its course through the Commons on June 23 the title of the Mental Welfare "Board" was changed to the Mental Welfare Commission, in response to a feeling that "Board" had a nineteenth-century tang about it. The membership of the Commission was increased from five to seven, with a requirement that at least one of the members should be a woman. The Opposition, with less success, sought to have two of the commissioners appointed on a full-time basis. The Secretary of State, Mr. J. S. MACLAY, restated his intention to appoint two full-time commissioners, but refused to write it into the Bill. He had three reasons for this decision, on which he said he had taken extensive advice and that medical opinion which he had consulted agreed.

Doctors on Mental Welfare Commission

It was accepted, and he intended to ensure, that the Commission should have at its disposal, both in its own membership and among its officers, an adequate number of doctors with the necessary qualifications and experience to enable it to discharge its duties effectively. There must be three doctors on the Commission, all of whom must have background and experience in psychiatry. In addition, under subsection (5), the Secretary of State had the responsibility of providing the Commission with such other medical staff as it required. These doctors would be comparable to the present deputy commissioners of the Board of Control. The number to be appointed would have to be discussed with the Commission from time to time; his intention was to start with at least three.

The second point was the independence of the doctors on the Commission. He had it in mind that the medical members should serve the Commission only; they would not, as the present Commissioners of the Board of Control were, be both Commissioners and medical officers in the Secretary of State's department. This was in line with the recommendation of the Dunlop Committee. There should therefore be no question of the medical commissioners being in any way susceptible to outside control from the Secretary of State because of the nature of their appointment. The third point was whether, to give this independence, it was necessary also to provide in the Bill that they should serve the Commission, and no one else, whole-time. The Opposition had agreed in the committee stage that one medical member should be a psychiatrist, serving the Commission on a part-time basis and giving the rest of his time to the hospital service. It was clearly desirable that the Commission should have a doctor who was facing the day-to-day problems of psychiatry in practice. The initial appointment of the other two commissioners he intended should be on a whole-time basis. It could, however, happen in future that a doctor who was regarded as the best person to be appointed might not be anxious to sever his connexion with his other work—he might, for example, wish to pursue his clinical work, or research, on a limited basis; or be a university teacher who did not wish to forgo altogether his academic work. It seemed undesirable to have in the Bill something that would forbid altogether an arrangement by which he could give, say, four-fifths of his time to the Commission and the rest to his own work. The flexibility in the membership of the Commission would make it possible at any time to substitute two part-time medical commissioners for one whole-time, and thus obtain more than the equivalent of a whole-time medical member.

Independence of Medical Commissioners

Dr. DICKSON MABON (Greenock, Lab.) came out as one instance of medical opinion that was not convinced by these arguments. He welcomed the fact that the principle behind the Opposition amendment had been conceded, that the independence of the commissioners was to be secured at least by administrative action, but held that if it was not written into the Bill the principle was completely undermined. The Government seemed to assume that the two commissioners would not be working at full pressure, which he did not accept for the foreseeable future. There were 20,000 patients in mental institutions, and about 6,000 mental defectives still in the queue and not yet accommodated. There would be a tremendous administrative inflow and outflow, an enormous volume of work in the next five years, and he could not see how the two commissioners would not be fully occupied.

Mr. MACLAY answered these, and other, arguments with the statement that there was no reason to be worried about the volume of work, because it was intended at present that the two medical commissioners should be full-time. If later it seemed desirable that one or more should not be full-time, sufficient part-time members could be appointed to do more than make up for the full-time appointments. On the point of independence, he was prepared to examine this carefully before the Bill was passed, and see whether a form of words could be found to make it clear that a part-time medical commissioner should not double that job with a job in the Scottish Office or another Government department. He had looked into it, and had not so far found an answer; the drafting of such a provision was not easy, and he could not give an absolute promise.

The Opposition amendment was rejected by 151 votes to 96.

Registration of Private Hospitals

Among other changes, an amendment was made to Clause 16, on the registration of private hospitals, requiring that before registration the Secretary of State should satisfy himself that the medical and nursing staff proposed was adequate and was suitably trained and qualified. It was also required (in an amendment to Clause 15) that a certificate of registration must specify the maximum number of persons who might be received at any one time in a private hospital. The certificate may also specify conditions as to the category of mentally disordered patients who may be received in the hospital. On Clause 27 (medical recommendations) there was some objection to a Government amendment requiring the two medical practitioners giving the two recommendations in support of an application for admission or a guardianship application to examine the patient separately if the patient or the nearest relative objected to the examinations taking place together, but it was eventually accepted.

In the debate on the third reading, Mr. MACLAY stated that the committee which he proposed to appoint to manage the State hospitals (for persons requiring treatment under conditions of special security) would be directly responsible to him and not part of the regional hospital arrangements. As he envisaged it, it would consist of a chairman, three consultant psychiatrists of standing (one of them, he hoped, of senior university status), a lawyer, and someone with local authority experience. If none of these persons was a woman he proposed to add one to the committee. In the general expansion of the service a major difficulty would be the rapid expansion of the number of skilled workers of all kinds. He sincerely hoped that more young doctors would be attracted to psychiatry, a lively and rapidly expanding specialty, in which there was ample opportunity for good men and women. Arrangements were in hand for meetings to be held in the autumn with the consultant psychiatrists in Scotland to discuss present trends and the best ways of making use of medical resources.

QUESTIONS IN THE COMMONS

Testing New Drugs

Mr. GEORGE DARLING (Sheffield, Hillsborough, Lab.) asked the Minister of Health on June 20 if he would introduce regulations to require that all new drugs be tested and

evaluated by a responsible body before they were offered for sale to the public. Mr. D. WALKER-SMITH said that, while there were no existing powers under which such regulations could be made, he was giving, and would continue to give, all the help and encouragement he could towards improvements in the present arrangements and facilities for clinical trials. The Central and Scottish Health Services Councils had agreed to extend the terms of reference* and membership of the Standing Joint Committee on the Classification of Proprietary Preparations to enable this Committee to assist.

Pneumoconiosis Claims

Dr. BARNET STROSS (Stoke-on-Trent, Central, Lab.) asked the Minister of Pensions and National Insurance to state the number of first claims for suspected pneumoconiosis in England and Wales during the last accountable year; how many of these received a clinical examination as well as examination by *x*-ray; how many were judged to be suffering; how many were rejected; and, of the latter, how many appealed and were after clinical examination successful. Mr. J. BOYD-CARPENTER stated that during 1959, 14,258 persons in England and Wales were *x*-rayed following a claim in respect of pneumoconiosis under the Industrial Injuries Acts, and of these 6,107 were referred for a clinical examination, but not all of these were examined in that year; 7,650 pneumoconiosis claimants, in whom the condition had not been previously diagnosed, received clinical examinations during 1959; of these 3.522 were found to be disabled by the disease. Among those clinically examined were 481 persons who had appealed against a disallowance based on a radiograph, and of these 36 were found to be disabled by the disease.

Occupational Deafness

Mr. R. E. PRENTICE (East Ham, North, Lab.) asked the Minister of Pensions and National Insurance what research was being conducted by his department into occupational deafness, with a view to its possible prescription as an industrial disease. Mr. BOYD-CARPENTER said that none was being done directly, but he was in touch with the research work on deafness now being carried out by the Medical Research Council. The Minister for Science had appointed a committee to examine the nature, sources, and effects of the problem of noise.

Mr. PRENTICE said that there were already in the United States and some European countries schemes for compensation for occupational deafness. Was it not a fact that the Ministry received claims under the Industrial Injuries Act from people who were made deaf at work and that those applications could succeed only if there had been an accident, and that the department had to reject many claims which were the result of genuine cases of deafness due to conditions at work? Mr. BOYD-CARPENTER replied that comparison with European schemes did not help much, because the Industrial Injuries Act was on a markedly different basis in many respects from most Continental schemes. Before a disease could be brought in under the Act it must comply with the provisions of Section 55, and he had no reason to believe that deafness did that.

Mortality from Smallpox and Vaccination

According to replies given to Mrs. JOYCE BUTLER (Wood Green, Lab.) no deaths from smallpox occurred in 1959 in England, Wales, or Scotland; one case of smallpox was notified in England. There were, however, two deaths in England and Wales from the results of vaccination: one was of a child aged 3 months and the other of a person aged 20 years. In Scotland there was one death from post-vaccinal encephalitis in 1957 (a male under 1 year), none in 1958, and two in 1959 (one male and one female, both under 1 year).

Relief of Pain at Childbirth

Dr. EDITH SUMMERSKILL (Warrington, Lab.) asked the Minister of Health which hospitals were testing the new automatic nitrous-oxide–oxygen machine for the relief of pain at childbirth; and whether the Minister had received a report through the Medical Research Council regarding the effectiveness of this machine. Mr. WALKER-SMITH replied that the new machine had been tried out at the Kingsbury Maternity Hospital and Oldchurch Hospital, Romford, before the Medical Research Council began consideration of the matter. He had not yet received a report from the Council, but he understood that preliminary investigations were in progress.

Assistants in General Practice

Mr. L. PAVITT (Willesden, West, Lab.) asked the Minister if he proposed to raise the grant for a trainee assistant in general practice from £775 to £1,150; and when an announcement about this matter might be expected. Mr. D. WALKER-SMITH answered that full acceptance of the Report of the Royal Commission on Doctors' and Dentists' Remuneration included acceptance of this recommendation. Discussions with the medical profession on the Government's offer to implement the Report as a whole as it stood were in progress, and he was not yet able to answer the last part of the question.

Mr. PAVITT also asked what was the present average salary paid to an assistant in general practice; what the Minister estimated this would be if the recommendations of the Pilkington Report were operated; and what he proposed to persuade employing doctors to implement these recommendations. Mr. WALKER-SMITH said that he had no information about the present average salary of assistants in general practice. Their conditions of employment were arranged by private contract between the principal and the assistant, and the Royal Commission recommended that this arrangement should continue. The last part of the question did not therefore arise.

*The terms of reference of the Standing Joint Committee have been extended as follows: "To advise on the circumstances in which clinical trials of new drugs not accepted as of proved therapeutic value, but for which *prima facie* evidence of therapeutic value is presented, should be encouraged; to recommend which products submitted to them for classification should undergo independent clinical trials; to assist manufacturers, if desired, in arranging such clinical trials for their products by giving guidance on the trials that should be carried out, including the agencies that might be used; and to assess the results of the trials as a preliminary to classification of the preparations."

Medico-Legal

ABNORMAL HUSBANDS AND CRUELTY

[FROM OUR LEGAL CORRESPONDENT]

Intention, or malignity, is an essential element in the matrimonial offence of cruelty. There can be no such cruelty if the accused spouse is of unsound mind and so does not know the nature and quality of his acts. Similarly, a spouse is not cruel who secretly embarks on a course of conduct, intending to conceal it from the marriage-partner, although when the conduct is discovered it results in grave nervous injury.

On May 2 the Court of Appeal dismissed an appeal against the refusal of a decree nisi on an undefended petition brought on the grounds of cruelty (Bohnel v. Bohnel [1960] WLR 590). The cruelty alleged by the wife was that her husband had constantly desired, and shown his desire, to dress like a woman. The parties were married in 1943, and, although the sexual relationship between the parties was cool, the husband managed to conceal his proclivities from his wife until 1955 when she discovered them by chance and suffered a nervous breakdown. In 1958 she made a second discovery of this behaviour, and there was a possibility of a recurrence of her nervous disorder. At her instigation the husband saw a doctor, who suggested treatment which might have controlled his impulses, but he took no treatment. The court held that, in view of the husband's attempts at concealment, it was impossible to find that he

had intended to injure his wife, or to say that he had deliberately pursued a course of conduct which he must have realized would be likely to cause her injury. Moreover, the treatment suggested would not have increased his sexual desire towards his wife and so would not have cured the marital difficulties, and therefore his failure to undergo treatment was not unreasonable. The charge of cruelty was not established.

Reasonable Apprehension of Injury to Health

Abnormality, in fact, is not cruelty; but it may affect the nature of conduct which, apart from the history of abnormality, would not amount to cruelty. A spouse petitioning for divorce on the grounds of cruelty must show some injury to health arising out of the conduct complained of. The mental health or normality of the respondent is thus a relevant consideration when deciding whether an apprehension of injury felt by the petitioner is reasonable or not: this principle was applied in a recent case.

On May 25, Mr. Justice Wrangham granted a decree nisi of divorce to Mrs. Constance Florence Robins of Stevenage, on the grounds of the cruelty of her husband (*The Times*, May 26). The parties were married in 1945, and since 1952 the husband had suffered from a series of mental illnesses, and had been a patient in a mental hospital for a time. There were allegations in the petition concerning certain unfounded accusations made by the husband against the wife. The court held, however, that this conduct arose out of the husband's lack of mental health, and that he genuinely believed in the truth of these statements, so that his conduct did not amount to cruelty. The finding of cruelty was based on an incident occurring on May 15, 1960, when the husband slapped his wife across the face, and, when their 12-year-old child screamed, he caught it by the throat. This assault was so slight as to have no effect on the wife's health. The court also held that, if the incident had occurred between sane and rational parties, it would not have given rise to a reasonable apprehension of injury; however, judged in the light of the husband's previous history, the assault did give rise to a reasonable apprehension of injury to the wife's health.

FALSE MEDICAL CERTIFICATES

[FROM OUR LEGAL CORRESPONDENT]

At the Carmarthen Magistrates Court on May 9, two doctors were fined £6 each on charges that they had each uttered six false medical certificates (*Western Mail*, May 10). At the same proceedings, a housewife, Mrs. Joyce Nancy Owens, aged 35, of Brewery Road, Carmarthen, was fined £14 on seven charges of obtaining sickness benefit for her husband by making false declarations. Mrs. Owens approached the doctors at different times between August 28, 1958, and October 22, 1959, representing that her husband was suffering from minor ailments when in fact he was at work. Relying on her representations, the doctors gave certificates without seeing her husband. By means of these certificates, Mrs. Owens obtained a total of £31 9s. in sickness benefit. Mrs. Owens's husband knew nothing of her going to the doctors. The doctors and Mrs. Owens pleaded guilty.

CORONERS' CASES

Dying Patient Sent Home

An inquest was held on April 7, at Macclesfield, to inquire into the death of a Miss Florence Griffin, aged 65. It was stated that the deceased, who lived alone and had no one to look after her, was taken ill at home. A neighbour called the police and Miss Griffin was found lying semi-conscious near her bed. Her doctor examined her and an ambulance was ordered to take her to hospital. The doctor said that the ambulance was directed to take the patient to the Macclesfield General Hospital, but apparently there was a misunderstanding and she was in fact taken to the West Park Hospital. On arrival she was lucid and was questioned and examined in the ambulance by one of the medical staff. He had no previous knowledge of her intended admission and received no history of the case. He made several unsuccessful attempts to get in touch with Miss Griffin's doctor whilst she was still in the ambulance. He concluded that the patient was well enough to be looked after at home and instructed the ambulance driver to take her home. He then succeeded in locating Miss Griffin's doctor, reported what he had done, and asked the doctor to visit her at home.

Miss Griffin's condition became worse on the journey and by the time the ambulance attendants had got her to her bedroom she was in a state of collapse and soon became comatose. Her doctor was called again and, as a result, the patient was taken back to the hospital and admitted. Death occurred five days later. Dr. Frank Aaron, the pathologist, said that the deceased had valvular disease of the heart and generalized arteriosclerosis. There was evidence of a recent cerebral vascular accident which had caused a patch of softening of the brain. Dr. Aaron added that even if Miss Griffin had been admitted straight away it would not have made any difference to the time of her death. The East Cheshire coroner, Mr. H. Sidebotham, said it was his job to say only how, when, and where Miss Griffin died; beyond that he did not need to go. He recorded a verdict of death from natural causes in accordance with the medical evidence (*Guardian*, April 8).

Universities and Colleges

UNIVERSITY OF OXFORD

Dr. Edith Bülbring, F.R.S., Reader in Pharmacology in the University, has been elected to a Professorial Fellowship at Lady Margaret Hall.

UNIVERSITY OF CAMBRIDGE

Dr. H. F. Grundy has been reappointed a University Lecturer in the Department of Pharmacology with tenure from January 1, 1961, to the retiring age.

Dr. L. G. Whitby has been appointed University Biochemist to Addenbrooke's Hospital in the Department of Biochemistry with tenure from July 1, 1960, for three years in the first instance.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At an Extraordinary Meeting of the Council of the College held on June 8, with Sir James Paterson Ross, Bt., President, in the chair, Professor Carl Semb, of Oslo, was admitted to the Honorary Fellowship of the College, after a citation had been made in his honour by Sir Clement Price Thomas.

Diplomas of Fellowship were granted to the following successful candidates:

T. E. Jeffreys, R. T. B. Jones, Delia M. H. H. Cothay, J. L. Somervell, J. R. F. Ingall, J. M. Dolphin, J. R. Kirkup, C. G. Keith, J. H. H. Webster, P. C. Anderson, L. J. Lawson, D. W. Atkinson, M. Swann, P. R. Hawley, M. A. Nelson, H. C. Smith, R. L. Agarwal, J. W. Eadie, D. M. Davies, D. MacG. Boyd, J. N. Cozens-Hardy, J. D. Sheils, M. N. Burhan, T. D H. Gray, J. A. O'Reilly, T. J. Aloysius, J. Considine, F. J. Ensell, M. R. Mynhardt, B. L. Talwar, J. S. Gupta, K. L. Hayes K. T. Jones, A. D. Lyall, R. N Mullick, C. V. Petersen, S. R. Chandrasekha, I. A. Le G. Ferguson R. L. Garner, J. N. Gibson, M. C. T. Morrison, S. R. Samsi, G. A. G. Scarlett, P. C. Bansal, A. P. Blower, B. W. Broadhurst, D. G. Calvert, J. F. Cullen, A. K. Dharbhaumik, I. S. Lister, P. Mazumder, M. P. A. Menon, P. J. Molloy, M. Sein, E. P. Simkin, D. Solomons, G. W Spragge. R. D. Upton, B. J. Bowden, E. R. Briant, G. R. Duncan, M. B. C. P. Gunawardene, J. Z. Handelsman, L. N. Hasso, J. D. Iswariah, D. R H. Kennedy, R. J. Kitchin, J. T. Kuruvila, M. Laurence, S. M Mahaluxmivala, T S. Mangat, A. K. Ommaya, R. A. Roxburgh, C. D. Sagar, M. El-Din Sedky, H. J. K. Vieyra, R. C. W. Williams, Ruth Wynne-Davies, J. G. Allman, R. C. Bennett, D. M. Burgess, G. V. P. Chamberlain, A. C. W. M. Da Roza, J. R. M. Davidson, A. C. B. Dean, B. Gampel, A. H. Hackett, R. M. Hollings. L. K. Jobbins, H. R. Johnson, D. M. King, F. W. Kwok, J. B. Lynch, R. S. McAlary, J. B. McFarland, B. V. Mehta, V. K. Pillay, D. J. Reid. K. FitzM. Ross, G. B. Smaill, M. P. Vaidya, I. H. Warner, M. O. Woo-Ming, S. B. Basnyat, S. V. Bhave, Cheung-Ping Chan, G. D. Chisholm, A. K. Dangarwala, A. Dev, W. G. Edwards, A. J. J. Emmett, J. I. H. Hadfield, I. M. Hamilton, L. Lenaghan, F. T. McDermott, M H. W. Mullerworth, B F. Reeves, J. S. Scougall, G. A. Syme, D. F Weinman, A. O Adesola, M. Balesegaram, K. A. Butler, D M. Essenhigh, H. J. H. Fry, G. R. Gibson, Ann E. Johnson, P. W. B. Lane, W. Leach, J. B. Morris, E. L. Parry, P. H. Smith.

Then followed the presentation of diplomas to those who had been successful in various examinations of the College during the past year. Parties from each of the medical schools were presented in turn to the President for receipt of the diplomas.

at his hands, and some 229 diplomates were presented in this way in the presence of an audience which filled the Edward Lumley Hall.

At the end of the ceremony the diplomates were addressed by Professor Carl Semb, and a vote of thanks to him was proposed by Mr. A. Dickson Wright.

At a meeting of the Council on June 9, with Sir James Paterson Ross, Bt., President, in the chair, the Lady Cade Medal was presented to Group Captain R. C. Jackson. Begley Prizes were presented to Dr. J. Barrett, of St. Thomas's Hospital Medical School, Dr. G. A. Hunter, of University College Hospital Medical School, and Dr. R. E. Robinson, of St. Mary's Hospital Medical School.

The following were co-opted to the Council for the year 1960–1, representing various branches of practice: *Ophthalmology*, Mr. T. Keith Lyle; *Otolaryngology*, Mr. C. Gill-Carey; *Gynaecology and Obstetrics*, Mr. H. G. E. Arthure; *Anaesthetics*, Dr. G. S. W. Organe; *Dental Surgery*, Professor M. A. Rushton; *General Practice*, Dr. John H. Hunt; *Radiology*, Professor D. W. Smithers.

Dr. Preston A. Wade, of New York, was appointed to deliver the second Watson-Jones Lecture.

The Mitchiner Medal for 1959 was awarded to Lieutenant-Colonel I. A. Walsh, and for 1960 to Major-General W. D. Hughes.

A Diploma of Membership was granted to C. J. Smallwood.

UNIVERSITY OF LONDON

Mr. J. B. Hume has been re-elected a member of the Senate by Convocation for the period 1960–4 as the representative of the graduates in medicine.

Dr. H. W. Bunjé has been nominated as representative of the University on the governing body of Battersea County Secondary School, and Dr. S. Gnessen as representative on the governing body of Brook House Secondary School.

Dr. Richard Creese has been awarded the William Julius Mickle Fellowship for 1959–60.

G. M. Heeley (Mirfield Grammar School) has been awarded the Mabel Sharman-Crawford Scholarship, and Patricia Lee (Gateshead Girls' Grammar School) the Bostock Scholarship for Women, both entrance scholarships to the Royal Free Hospital School of Medicine.

UNIVERSITY OF SHEFFIELD

Dr. G. Meachim has been appointed a full-time temporary Lecturer in Pathology.

Dr. Jillian Horner has resigned from her appointment as Research Assistant in Medicine.

ROYAL COLLEGE OF SURGEONS IN IRELAND

On June 20 the Licence in Midwifery and Surgery of the College was conferred upon M. A. L. Tansey.

ROYAL AUSTRALASIAN COLLEGE OF PHYSICIANS

At a meeting of the General Body of Fellows of the College held in Melbourne on May 25, the following were elected and admitted to Fellowships of the College: *Under Article 44:* Dr. F. W. A. Clements and Professor F. C. Courtice, of New South Wales; Dr. D. O. Shiels, of Victoria, and Sir Geoffrey Sydney Todd, of England. *Under Article 42:* Dr. B. A. D. Curtin, Dr. R. I. Eakin, Dr. E. J. Halliday, Dr. G. L. McDonald, and Dr. J. R. Sands, of New South Wales; Dr. A. V. Jackson, Dr. H. I. Jones, Dr. L. Murphy, Dr. H. P. Taft, Dr. H. E. Williams, and Dr A. Wynn, of Victoria; Dr. R. A. Burston, Dr. J. S. Covernton, Dr. A. K. Grant, Dr. R. Hecker, and Dr. J. M. McPhie, of South Australia; Dr. P. L. Dorney and Dr. F. R. T. Stevens, of Tasmania; Dr. G. F. Hall and Dr. W. J. Smith, of New Zealand.

The following candidates, who were successful at an examination held in Australia, were admitted to Membership of the College on May 23: Dr. O. Appenzeller, Dr. A. G. G. Bennett, Dr. L. Brenner, Dr. D. S. Child, Dr. J. M. Duggan, Dr. N. D. Gallagher, Dr. B. Haneman, Dr. A. M. Lloyd, Dr. M. S. Owen, Dr. B. J. Pascoe, Dr. R. A. Royle, and Dr. J. D. Wingfield, of New South Wales; Dr. H. G. Burger, Dr. K. Catt, Dr. B. S. Faragher, Dr. J. E. Fitzgerald, Dr. J. Hansky, Dr. A. K. Lethlean, Dr. I. G. Lyall, Dr. J. F. O'Callaghan, Dr. S. F. Phillips, Dr. J. G. Sloman, and Dr. R. R. W. Townley, of Victoria; Dr. J. T. Andrews, Dr. G. T. Ey, and Dr. A. J. Watson, of South Australia; Dr. K. R. Hayes and Dr. K. P. Kennedy, of Queensland; Dr. B. R. Beveridge and Dr. B. A. Kakulas, of Western Australia. *Under Article 37:* Dr. K. F. Anderson, of South Australia, Dr. G. M. Watson, of New South Wales, and Dr. Saul Wiener, of Victoria.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **June 11** (No. 23) and corresponding week 1959.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1960					1959				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	3	0	1	0		4	4	1	0	4
Dysentery ..	757	103	191	20	3	938	111	297	17	5
Encephalitis, acute	2	1	0	0		2	0		0	
Enteric fever:										
Typhoid ..	3	2	0	0		2	1	1	0	1
Paratyphoid ..	2	0	0	1		3	1	3 (B)	0	1 (B)
Food-poisoning ..	343	65	99	1		437	83	17	0	
Infective enteritis or diarrhoea under 2 years				8	24				8	35
Measles*	2,477	146	57	7	15	13,521	585	324	376	182
Meningococcal infection	15	1	11	0	1	17	2	10	0	1
Ophthalmia neonatorum	13	1	0	0		26	3	13	0	
Pneumonia† ..	220	11	157	0	2	194	5	136	1	
Poliomyelitis, acute:										
Paralytic ..	4	1	0	} 1	8	18	10	3	} 0	
Non-paralytic ..	0	0	1			4	1	2		
Puerperal fever§ ..	149	24	11	0		187	17	10	1	
Scarlet fever ..	409	21	36	17	16	925	53	90	32	13
Tuberculosis:										
Respiratory ..	382	29	70	13		475	54	73	17	
Non-respiratory	58	4	21	2		64	4	21	0	
Whooping-cough	1,150	86	217	7	73	642	31	97	22	86

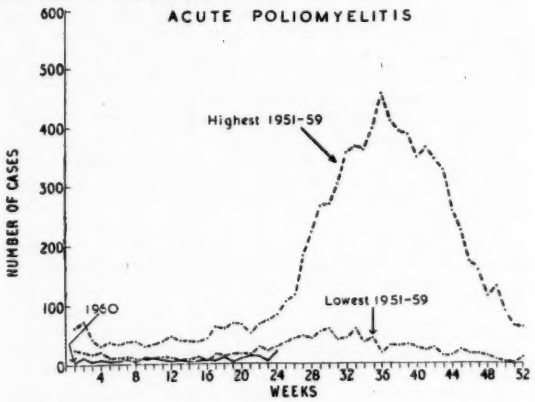
DEATHS	1960					1959				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0	0	0	0	0	0	0
Dysentery ..	1	0		0		1	0		0	
Encephalitis, acute		7		0	0		0			0
Enteric fever ..	1	1	0			0	0	0	0	
Infective enteritis or diarrhoea under 2 years	6	0	4	0	0	9	0	3	0	1
Influenza	9	1	1	0	0	6	0	0	0	0
Measles		0	0	0	0		0	0	0	0
Meningococcal infection		0	0				0	0		
Pneumonia ..	410	29	12	18	6	332	30	18	11	11
Poliomyelitis, acute	0	0		0	0	0	0		0	0
Scarlet fever ..		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory ..	} 61	3	5	0	0	} 56	3	2	3	0
Non-respiratory			0	0	0		1	0	0	0
Whooping-cough	0	0	0	0	0	0	0	0	0	0
Deaths 0–1 year	272	22	36	10	12	291	25	32	7	13
Deaths (excluding stillbirths) ..	8,686	677	505	135	184	8,273	664	536	112	159
LIVE BIRTHS .	13,998	1214	1070	300	360	15,053	1282	1075	297	394
STILLBIRTHS ..	261	15	29			295	20	25		

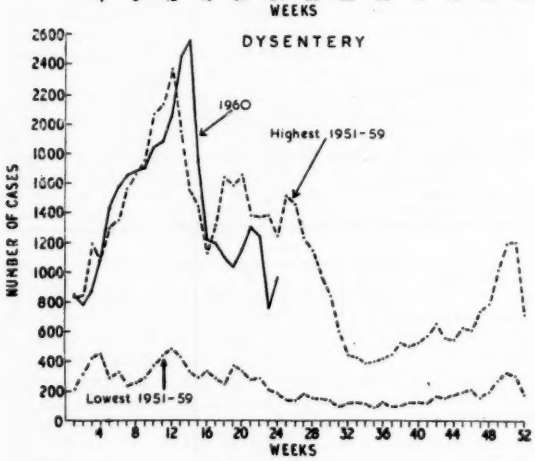
* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

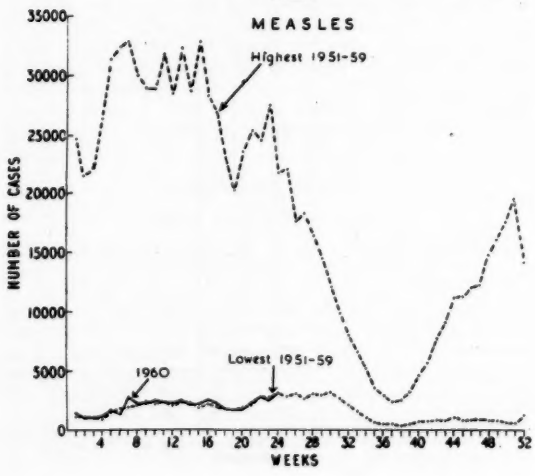
Vital Statistics

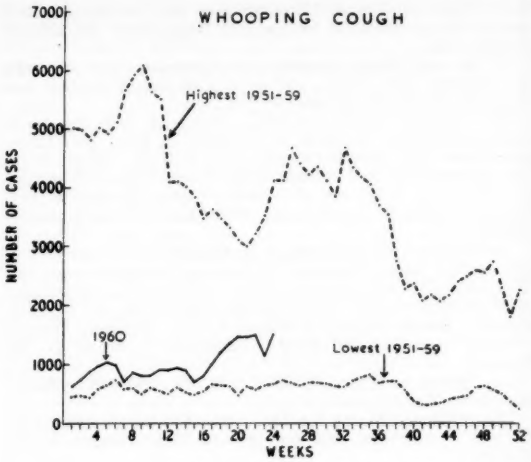
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1951–9 are shown thus ------, the figures for 1960 thus ———. Except for the curves showing notifications in 1960, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available.

	Week Ending June 11	Week Ending June 18
Dysentery		
Berkshire	19	**28**
Windsor R.D.	9	**20**
Durham	20	**42**
Seaham U.D.	7	**29**
Hertfordshire	8	**23**
Welwyn Garden City U.D.	1	**13**
Lancashire	119	**155**
Liverpool C.B.	29	**20**
Urmston U.D.	1	**20**
London	103	**130**
Camberwell	5	**16**
Islington	22	**27**
Norfolk	25	**22**
Norwich C.B.	12	**18**
Surrey	20	**34**
Carshalton and Warlingham U.D.	10	**11**
Dorking and Horley R.D.	0	**15**
Yorkshire North Riding	12	**24**
Flaxton R.D.	5	**17**
Yorkshire West Riding	74	**107**
Bradford C.B.	11	**33**
Leeds C.B.	13	**27**
Sheffield C.B.	16	**21**
Glasgow	104	**75**
Food poisoning		
Hampshire	4	**75**
Ringwood and Fordingbridge R.D.	0	**72**
Gloucestershire	43	**97**
Gloucester R.D.	31	**81**
Paratyphoid fever		
Glasgow	2	**5**
Measles		
Nottinghamshire	182	**264**
Nottingham C.B.	141	**177**
Lancashire	742	**1,147**
Liverpool C.B.	221	**383**
Manchester C.B.	82	**124**
Acute poliomyelitis		
London	1	**5**
Warwickshire	0	**4**
Birmingham C.B.	0	**4**

Medical News

Queen Square Centenary Banquet

As a climax to the centenary celebrations of the National Hospital last week, the Chartered Society of "Queen Square" gave a banquet at the Mansion House on June 24. Under the chairmanship of Sir ERNEST GOWERS, the younger son of the famous neurologist and a former chairman of the Hospital, some 280 persons, including the LORD MAYOR OF LONDON, Sir EDMUND STOCKDALE, and the LADY MAYORESS, attended. Thirty-five countries were represented. The toasts were "The Lord Mayor and the Corporation of London and the Sheriffs," "The National Hospital," and "The Guests," proposed respectively by Sir ERNEST GOWERS, Professor G. H. MONRAD-KROHN, of Oslo, and Dr. MACDONALD CRITCHLEY. The responders were the LORD MAYOR, Sir JOHN WOODS (the present chairman of the National Hospital) and for the guests Mr. GEOFFREY JOHNSON SMITH, M.P. for Holborn and St. Pancras, and Dr. PERCIVAL BAILEY, of Chicago.

B.M.A. Reception for Queen Square Centenary

The Council of the British Medical Association gave a midday reception on June 24 for overseas visitors to the centenary celebrations of the National Hospital for Nervous Diseases. The reception followed the eleventh Victor Horsley Memorial Lecture in the Great Hall of B.M.A. House which was delivered by Professor N. M. DOTT on "Brain, Movement and Time," and is printed on p. 12 of the *Journal*. At the reception official delegates from many overseas countries and distinguished foreign neurologists were received by Sir ARTHUR THOMSON. The National Hospital itself, the Royal Colleges, the Royal Society, and many other societies and organizations were well represented, and it was particularly pleasant to see members of Victor Horsley's family and friends—including his son-in-law, Mr. E. S. G. ROBINSON, and Sir ARCHIBALD GRAY, one of the famous surgeon's ex-students.

Heinz Fellowships of British Paediatric Association

H. J. Heinz Company, Ltd., have endowed three types of annual Fellowship in paediatrics which will be administered by the Nuffield Foundation in conjunction with the British Paediatric Association. The three types of Fellowship are as follows:

(1) To enable a young paediatrician from any part of the Commonwealth overseas to spend six to eight weeks visiting centres in the United Kingdom, and to attend the Annual Meeting of the B.P.A. (2) To enable a young paediatrician in training in any part of the Commonwealth overseas to spend one year of postgraduate study in paediatrics, child health, or paediatric preventive medicine at approved centres in the United Kingdom. (3) To enable a British paediatrician of registrar, senior registrar, or consultative status to spend a short period at some overseas centre to study a particular problem. Details and application forms—which must be returned by September 1—may be obtained from Mr. L. FARRER-BROWN, C.B.E., The Nuffield Foundation, Nuffield Lodge, Regent's Park, London, N.W.1.

Jodrell Chair of Physiology, University College, London

Mr. A. F. HUXLEY, M.A., F.R.S., reader in experimental biophysics in the University of Cambridge, has been appointed to the Jodrell Chair of Physiology tenable at University College, London. He succeeds Sir LINDOR BROWN, F.R.S.

Mr. Huxley, who is 42, was educated at University College School, Westminster School, and Trinity College, Cambridge, where he took a First in the Natural Sciences Tripos. The war interrupted his clinical studies at Addenbrooke's Hospital, Cambridge, and University College Hospital, and he did operational research for Anti-Aircraft Command from 1940 to 1942, and for the Admiralty from 1942 to 1945. He returned to the Physiological Laboratory, Cambridge, as demonstrator from 1946 to 1950, and assistant director of research from then till he took up his present position in 1959. He was Research Fellow of Trinity College from 1941 to 1952, and Staff Fellow from then to 1960. His earlier research work was on isolated fibres from squid and crab, and on isolated myelinated fibres. Since 1952 he has done research on muscle, using optical and electrical methods on isolated fibres from various animals. He was elected F.R.S. in 1955. His publications include papers in the *Journal of Physiology*.

Wolfson Research Professor of Royal Society

Dr. DOROTHY HODGKIN, F.R.S., university reader in *x*-ray crystallography, and fellow of Somerville College, Oxford, has been appointed as the first holder of the Wolfson Research Professorship of the Royal Society which was endowed earlier this year.

[J. R. V. Johnson

Dr. Hodgkin, who was born in Cairo, was educated at John Leman School, Beccles, and Somerville College, Oxford, where she read chemistry from 1928 to 1932 in the final honours school of natural science. She worked at Cambridge for her Ph.D. with J. D. Bernal, and began work on sterols, proteins, and other natural products. She returned to Somerville in 1934, first as research fellow and later as official fellow and tutor in chemistry. She retired from the tutorship when she took up her present position. She became F.R.S. in 1947 and was awarded the Royal Medal in 1957. Her principal researches have been concerned with the determination of molecular structures by *x*-ray analysis, particularly penicillin and vitamin B_{12}. She has also worked on cholesterol, calciferol, and various proteins, insulin in particular.

Family Planning Medical Advisory Group

In recognition of the increasing scope and responsibilities of the family planning movement, the Family Planning Association have set up a medical advisory committee under their president, Sir RUSSELL BRAIN. The membership is as follows:

Sir DUGALD BAIRD, Sir ANDREW CLAYE, Mr. DONALD FRASER, Dr. J. A. FRASER ROBERTS, Professor DOUGLAS HUBBLE, Mr. IAN JACKSON, Sir AUBREY LEWIS, Professor NORMAN MORRIS, Professor W. C. W. NIXON, Sir JAMES PATERSON ROSS, Mr. JOHN STALLWORTHY, Dr. G. I. M. SWYER, and Mr. JOHN SUTHERLAND.

Doctors in South Africa

A meeting to discuss the effect on the medical profession of racial discrimination in South Africa was held recently in B.M.A. House and attended by about 50 people.

The chairman was Dr. DAVID PITT, and the meeting was first addressed by Mr. NORMAN PHILLIPS, foreign news editor of the *Toronto Star*, who had himself been detained under the recent South African emergency regulations. Dr. ELEANOR ETTLINGER suggested that the medical profession should afford facilities for one or more non-European South Africans to study medicine in the United Kingdom, since all South African medical schools but one are now closed to non-European students. A motion was then carried that an organization should be set up called "Medical Committee against Racial Discrimination in South Africa," with the following objects: to support South African doctors and medical workers opposing Apartheid, and to obtain and publish—both in Great Britain and in South Africa—information relevant to the medical profession about the situation there. The meeting stressed the importance of working through and together with existing medical associations and organizations. Details may be obtained from Dr. ELEANOR ETTLINGER, 20, Lansdowne Crescent, London, W.11.

Society of Apothecaries

The Gold Medal in Therapeutics of the Worshipful Society of Apothecaries of London is to be bestowed upon Sir TUDOR THOMAS "in recognition of his outstanding services in the field of corneo-plastic surgery."

"Chemotherapy Review"

British and Overseas Pharmacy and Medicine, first published in its original form by the British and Colonial Druggist, Limited, in the 1880's, has changed its name to *Chemotherapy Review*.

Royal Society of Health Council

Dr. J. J. O'DWYER, chief medical officer, Unilever Ltd., has been elected, and Dr. E. HUGHES, Medical Officer of

Health, Reading, re-elected, to the Council of the Royal Society of Health.

"Family Doctor"

The July issue of *Family Doctor* is now available, price 1s. 6d. It includes articles on fibroids by Mr. ELLIOT PHILIPP, on tennis elbow by Mr. W. E. TUCKER, and on travel sickness by Dr. E. J. TRIMMER.

In Brief

The Royal College of Nursing will, in future, admit both male and female nurses who are on any of the recognized registers. Hitherto membership has been limited to general trained State-registered women nurses.

In Quebec's provincial elections a programme which included a proposal to establish a hospital insurance plan has brought the Liberal Party to power after the Union Nationale's rule of 16 years.

A Mozambique baobab, or monkey-bread tree, carved with Dr. David Livingstone's initials, has been declared a national monument by the Portuguese authorities. In Livingstone's *Family Letters* (reviewed on p. 37) he says that in 1853 the tree was 85 ft. in circumference, 60 ft. high, and that "its reddish colour makes it look more like a mass of red granite than a tree."

People in the News

Professor C. G. ROB, professor of surgery at St. Mary's Hospital Medical School, has been appointed to the chair of surgery, University of Rochester, New York, from September 30.

COMING EVENTS

Medical Film Festival.—July 5–7, British Council Film Theatre, Hanover Street, London, W.1. Details from the sponsors, *British Journal of Clinical Practice*, 171, New Bond Street, London, W.1 (HYD 7845).

Royal College of Surgeons of England.—Special lecture, Professor G. D. ROBB (Sims Commonwealth Travelling Professor): "Differential Incidence of Surgical Conditions as Between Maori and White People." July 12, 5 p.m., at the College, Lincoln's Inn Fields.

Bertram Louis Abrahams Lecture.—Professor H. BARCROFT, F.R.S.: "Nervous Control of Cutaneous Vessels," July 12. Details on advertisement page 63.

B.B.C. Radio: Royal Society Tercentenary.—Third programme talks during the Society's celebrations include, on July 25, "Genes and Atoms" (Dr. F. H. C. CRICK, F.R.S.); July 26, "Problems of Growth and its Control" (Professor M. ABERCROMBIE, F.R.S.); July 27, "Brain and Body" (Professor G. W. HARRIS, F.R.S.).

University of Glasgow and R.F.P.S.—"Recent Advances in Clinical Medicine," September 12–23. Details of advanced course on advertisement page 63.

NEW ISSUES

ARCHIVES OF DISEASE IN CHILDHOOD

Forty Years of Nephrosis in Childhood. David Lawson, Alan Moncrieff, and Wilfrid W. Payne.
Poisoning Accidents in Childhood. T. McKendrick.
Megaloblastic Anaemia of Infancy in Jamaica. J. E. MacIver and E. H. Back.
Congenital Thrombocytopenic Purpura. K. Hugh-Jones, P. A. Manfield, and H. F. Brewer.
Neurofibromatosis (von Recklinghausen's Disease) of the Vertebral Column. E. C. Allibone, R. S. Illingworth, and T. Wright.
Teratoma of the Neck. Reuben Silberman and Inez R. Mendelson.
Amoebic Liver Abscess in African Children. Joan Scragg.
Periprostatic Haematoma and Prostatic Abscess in the Neonatal Period. D. Innes Williams and Antonio G. Martins.
Generalized Bronchiectasis Associated with Deficiency of Cartilage in the Bronchial Tree. Howard Williams and Peter Campbell.
Symmetrical Peripheral Oedema in Infants. H. Everley Jones.
Paediatric Pathology Club.
Book Reviews.

Volume 35, No. 180. (Bi-monthly; £4 4s. annually.)

OPHTHALMIC LITERATURE FOR 1959

Volume XIII, No. 4 (2179–3282). (Quarterly; £4 4s. annually. Combined with *British Journal of Ophthalmology*, £9.)

Abstracts of World Medicine.—Issued in the first week of each month, this journal contains abstracts of important papers selected from the current medical literature of the world. Annual subscription £4 4s.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, July 4

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Professor C. Bruce Perry: Aetiology and Prevention of Acute Rheumatism.

Wednesday, July 6

●INSTITUTE OF CHILD HEALTH.—At Hospital for Sick Children, Great Ormond Street, London, W.C., 5 p.m., Alex Simpson Smith Lecture by Professor Norman Dott: Medulloblastoma Cerebelli.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., open lecture by Dr. I. S. Longmuir: Some Applications of Polarography to Hypothermia.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Dr. R. W. Riddell: Laboratory Diagnosis of Fungous Infection.
ROYAL FREE HOSPITAL, Gray's Inn Road, London, W.C.—5.15 p.m., Dr. John B. Stanbury (Boston): Cretinism as an Inborn Error of Metabolism.
SOCIETY OF MEDICAL OFFICERS OF HEALTH: HOME COUNTIES BRANCH.—2.30 p.m., Tour of Rural Life Museum and new University buildings at Reading.

Thursday, July 7

INSTITUTE OF NEUROLOGY.—5.30 p.m., Dr. G. Milton Shy (Bethesda, U.S.A.): Recent Studies in Familial Periodic Paralysis.
ROYAL SOCIETY OF HEALTH.—At Town Hall, Barrow-in-Furness, 10.15 a.m., Dr. L. Robertson: Brucella Organisms in Milk; Dr. R. F. L. Logan and Mr. Gordon Forsythe, B.A.: Measuring a Town's Health in 1960—An Appraisal of Indices which may help Local Health Care Administrators.

Friday, July 8

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. L. Livingstone: clinical demonstration
MIDLAND CENTRE FOR NEUROSURGERY, Holly Lane, Smethwick, near Birmingham.—8 p.m., Dr. A. Huber (Zurich): Eye Symptoms in Brain Tumours.

Saturday, July 9

CAMBRIDGE UNIVERSITY MEDICAL SCHOOL.—At Addenbrooke's Hospital, Cambridge, Symposium on Infectious Diseases, 10.30 a.m., Dr. D. M. T. Gairdner, Immunization in Childhood; 11.30 a.m., Dr. L. B. Cole, Diagnosis and Treatment of Tetanus; 12.15 p.m., Dr. D. Cameron, Glandular Fever; 2.30 p.m., Dr. R. M. Fry, Streptococcal Infections; 3.15 p.m., Dr. F. G. J. Hayhoe, Investigation of Unexplained Pyrexia.

APPOINTMENTS

BIRMINGHAM REGIONAL HOSPITAL BOARD.—K. L. G. Nobbs, M.B., B.S., M.R.C.P.Ed., Whole-time Consultant Physician with experience in Geriatrics to Birmingham (Mental B) and Selly Oak Groups of Hospitals.
LIVERPOOL REGIONAL HOSPITAL BOARD.—D. F. MacCarthy, M.Ch., Whole-time Senior Casualty Officer to Chester and District Hospital Management Committee (*corrected announcement*).
MIDDLESEX HOSPITAL London, W.—L. P. Le Quesne, D.M., F.R.C.S., and R. T. Turner Warwick, D.M., F.R.C.S., M.R.C.P., Consultant Staff as Assistant Surgeons.
NORTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD.—C. A. Simmons, B.M., B.Ch., F.R.C.S., M.R.C.O.G., Consultant Obstetrician and Gynaecologist, City of London Maternity Hospital and honorary appointment at the Royal Northern Hospital; H. N. O'Donoghue, M.B., B.Ch., D.O., Assistant Ophthalmologist (S.H.M.O.), King Edward Memorial Hospital, Ealing; M. Feiwel, M.B., B.Chir., M.R.C.P., Consultant Dermatologist, Paddington General Hospital and St. Charles' Hospital.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Adderley.—On June 17, 1960, to Jean, wife of David Adderley, of "The Grove," 91, Belmont Hill, London, S.E., a brother for Nicholas, Martin, Ruth, and Simon—John Edward.
Lambie.—On June 16, 1960, at Kowloon, Hong Kong, to Lily, wife of Dr. J. Lambie, a sister for Jacqueline.
Smith.—On June 20, 1960, at St. David's Hospital, Cardiff, to Helen, wife of William G. Smith, M.D., a brother for Heather.

DEATHS

Flett.—On June 5, 1960, at Gairloch, Wester Ross, accidentally drowned, Hugh Munro Flett, M.B., Ch.B.
Gillies.—On June 7, 1960, Douglas Wilson Gillies, T.D., M.B., Ch.B., of Springfield, Keighley, Yorks.
Hayward.—On June 7, 1960, at Glengairn Old School, Ballater, Aberdeenshire, Marjorie Florence Hayward, M.B., B.S.
Millar.—On June 4, 1960, at Crowborough, Sussex, Catherine Millar, L.R.C.P.&S.Ed., L.R.F.P.S., late of Edinburgh, aged 87.
Rayment.—On June 5, 1960, Frederick William Rayment, M.B., Ch.B., of the Old Rectory, Stanton St. Bernard, near Marlborough, Wilts, aged 77.
Shield.—On June 6, 1960, at his home, 43, Charlton Park, Keynsham, Somerset, Hubert Shield, *M.C.*, T.D., M.B., B.S., Major, R.A.M.C., retired.
Tonks.—On June 5, 1960, at Woodend Hospital, Aberdeen, Myles Denison Boswell Tonks, M.R.C.S., L.R.C.P., of St. James's, Ballater, Aberdeenshire.
Varian.—On June 8, 1960, at Duncliffe, Totnes, Devon, Amos George Varian, M.D.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Excessive Salivation

Q.—*I have a patient who continually dribbles saliva, causing excoriation of the angle of the mouth and of the chin. The salivary apparatus is otherwise normal. Belladonna dries the mouth without halting the flow. Have you any suggestions?*

A.—Excessive excretion of saliva is most often reflex in origin and is usually the result of a lesion in the upper gastro-intestinal tract. Therefore, although it is stated that the salivary apparatus is otherwise normal, it would be important to be certain that adequate investigation for any pathological condition of the mouth, throat, oesophagus, stomach, and duodenum had been carried out. Carious teeth, for example, are sometimes a cause of excessive salivation. Lesions of the oesophagus, such as achalasia or ulceration, are other possible causes. One assumes that the patient is not suffering from post-encephalitic Parkinsonism and is not receiving a mixture containing drugs such as iodides or mercury, which may cause an increase in the flow of saliva. The first approach to treatment should be a search for the cause along these lines and appropriate treatment for whatever condition is found. If this has already been done then the belladonna alkaloids or their analogues are usually the most effective drugs for the treatment of excessive salivation, but the amount required is often much larger than the ordinary pharmacopoeial dose and the other side-effects are frequently more uncomfortable than the salivation. Other drugs are unlikely to be helpful if belladonna is inadequate dosage has not been effective. If all else fails the possibility of a course of local radiotherapy to the salivary glands might be considered.

Backache After Disk Operation

Q.—*What causes persistent backache after an otherwise successful partial laminectomy for slipped disk? How long may such discomfort be expected to last? What treatment is recommended?*

A.—There are two aspects to the causation of persistent backache after operation for disk prolapse. When the operative exposure is extensive and includes removal of spinous processes, interspinous ligaments, or interarticular joints, instability results and backache is a common symptom. Because of this the inter-laminal approach has become popular. A disk which has prolapsed has also usually collapsed. This upsets the mechanics of the posterior joints and the hydraulic joint of the disk itself is also mechanically deranged. These factors are the cause of backache. The operation does nothing to remedy this defect.

Treatment is, in the first place, by the avoidance of weight lifting and stooping and, when necessary, the wearing of a corset. If—and it is uncommon—such measures fail to reduce the backache to small proportions spinal fusion is indicated. Although there are surgeons who advocate spinal fusion as a routine part of disk removal, the infrequency of severe backache after this operation seems to make this unnecessary.

Serum Transaminase Estimation

Q.—*What is the best method, suitable for a small laboratory, for the estimation of serum glutamic oxaloacetic transaminase?*

A.—A method for estimating serum transaminases suitable for use in a small laboratory with only an ordinary photoelectric absorptiometer is that described by Mohun and Cook.[1] The procedure is extremely simple, and in the writer's hands has provided most useful information about patients with coronary infarction and liver disease. The estimations of the two transaminases differ mainly in the compositions of the substrate, and it is no more difficult to provide estimations of both glutamic oxaloacetic transaminase and glutamic pyruvic transaminase than one only. The method is extremely straightforward and is well within the competence of the average technician. The writer is convinced that if one of these transaminases is to be estimated it is well worth while making provision for the estimation of the other, because the two together give far more useful information than either alone, particularly in liver disease and glandular fever.[2–5]

The preservation of the substrates for a few weeks is quite simple, but it is much more convenient to prepare half a litre or so, distribute it in tubes each containing 10–20 ml., sufficient for a dozen analyses, and freeze the whole lot in a −20° C. ice-cream conservator or deep-freeze unit. If this can be done it is very easy to take out a tube of substrate and run a set of transaminase determinations when wanted.

REFERENCES

1 Mohun, A. F., and Cook, I. J. Y., *J. clin. Path.*, 1957, **10**, 394.
2 De Ritis, F., Coltorti, M., and Giusti, G., *Clin. chim. Acta*, 1957, **2**, 70.
3 —— —— —— *Lancet*, 1958, **2**, 214-5.
4 Rosalki, S. B., *Proc. roy. Soc. Med.*, 1960, **53**, 199.
5 —— Gwyn Jones, T., and Verney, A. F., *Brit. med. J.*, 1960, **1**, 929.

Idiopathic Narcolepsy

Q.—*Is amphetamine still the best drug in the treatment of idiopathic narcolepsy? Have recent advances thrown any light on the aetiology of this disease? Are there any verified cases of spontaneous permanent cure?*

A.—Although amphetamine or dextro-amphetamine is the most efficacious drug in many sufferers from idiopathic narcolepsy, in some ephedrine is more effective. There does not seem to be any special danger in the long continued use of amphetamine. The aetiology of the "idiopathic" disease still remains unknown, and, so far as I know, recent advances in knowledge of brain metabolism have not yet elucidated this problem. There are some patients in whom treatment can be stopped and they remain free of attacks for long periods, but it is doubtful whether this should be called a permanent cure.

Chronic Anaemia

Q.—*A young woman's haemoglobin has been between 75% and 80% for six months in spite of ferrous sulphate and gluconate in usual oral dosage. She has no symptoms, other than some tiredness in the evening, and her periods are not excessive. Should something be done to raise the Hb level and, if so, what?*

A.—The haemoglobin level of between 75% and 80% in a young woman is clearly pathological. The commonest reason for this is chronic haemorrhage, and this is the most likely cause in the present instance. It is perfectly possible for the patient to be losing unusually large amounts of blood at her periods without her being aware that the loss is abnormal. However, chronic haemorrhage is not the only reason for chronic anaemia in a young woman, and if it is certain that she has been really taking the prescribed iron regularly, then the cause for the anaemia needs to be investigated. Amongst possible causes is the malabsorption syndrome in which the absorption of iron from the intestine is often impaired.

Transplanted Ureters and Rectal Leakage

Q.—*A girl aged 14 has had transplantation of the ureters into her colon. She manages extremely well and is very active, but there is some leak and a consequent urinous smell. What can be done?*

A.—Incontinence after the implantation of the ureters into the colon may be due to poor capacity of the rectum, impaired sensitivity of the rectal ampulla failing to indicate to the patient when the rectum is full, or weak anal sphincters. The first two conditions can be relieved by emptying of the rectum at decreasing intervals until the period is reached when the patient remains dry; then the

interval can be gradually increased, provided the patient remains dry. The weak sphincter muscles can be strengthened by exercises similar to those which have proved so successful in urethral incontinence. They may be supplemented by faradic stimulation to these muscles and the muscles of the floor of the pelvis.

The urinous smell is due to bacterial decomposition of the components of the urine, mainly of urea by the urea-splitting organisms, but also the aromatic substances are responsible to some extent. Thus scrupulous cleanliness and frequent changes of underclothes and diapers is essential. No satisfactory apparatus has been devised to keep these patients dry. Diet and deodorants are also unsatisfactory.

Cholesteroluria

Q.—*Under what conditions are large quantities of cholesterol excreted in the urine?*

A.—Normal urine contains only a small quantity of cholesterol, approximately 1 mg./l.[1] It is present partly as crystals in the urinary deposit and partly in solution. The origin of the greater part of this cholesterol is from the mucus secreted by the glands of the mucosa of the urogenital tract.[2] A little is derived from the plasma as lipoprotein present in small quantities in normal urine. There is no correlation between the amount of cholesterol in the blood and urine.

When a large amount of cholesterol is found in the urine it generally arises from pathological conditions of the urinary tract.[3] The deposit contains large irregular plate-shaped crystals, some with notched corners, which are colourless and transparent. These crystals are seen in patients with cystitis and pyelitis. Cholesterol in the urine is increased in nephrosis and with albuminuria, possibly from lipoproteins. The quantity is small and is not correlated with the degree of albuminuria. A cholesterol calculus resembles the cystine type and is extremely rare.

REFERENCES

1 Cook, R. P. (Editor), *Cholesterol, Chemistry, Biochemistry, and Pathology*. 1958, 1st edition. Academic Press, New York.
2 Kayser, F., and Balat, R., *Bull. Soc. Chim. biol.*, 1952, **34**, 806.
3 Hawk, P. B., Oser, B. L., and Summerson, W. H., *Practical Physiological Chemistry*, 1954, 13th edition. Churchill, London.

Fructose in Diabetes

Q.—*What are the uses of fructose (laevulose) in treatment? Has it any advantage over glucose (dextrose) for diabetes?*

A.—Fructose probably has no advantage over glucose in routine treatment; when given by mouth it is converted to glucose. There is, however, some evidence for the value of intravenous fructose in diabetes, and the subject was reviewed in an annotation in the *Journal* a few years ago.[1] It has been known for a long time that the diabetic organism can utilize fructose more efficiently than glucose, presumably owing to the fact that insulin is not required in its metabolism. When given as a 10% infusion to diabetics the sugar is utilized satisfactorily by the liver and peripheral tissues, though so far as is known this form of treatment has not been widely adopted.

REFERENCE

1 *Brit. med. J.*, 1954, **1**, 510.

Superficial X-ray Therapy in Children

Q.—*Is there any risk in giving a child three small surface doses of X rays at monthly intervals for recurrent dermatitis?*

A.—There is a risk of even small doses of *x* rays affecting the growing ends of bones, endocrine glands, and other sensitive and vital growing structures in a child, and *x*-ray therapy should not be employed unless it is essential. This is particularly true of a chronic or recurrent affection even though dosage may be from as low a kilovoltage as 50 or 60 and is unfiltered. Grenz rays, from a kilovoltage of 2 to 10, are probably safe, since there is no significant penetration.

Carcinogenic Risk of Tar Ointment

Q.—*Is there a carcinogenic risk in using tar ointment in a water-soluble base as an application for recurrent eczema in a child?*

A.—It seems unlikely from clinical experience that there is any significant risk here. Accounts in the world literature of two or three patients in whom a tar epithelioma has been reported from this source are not very convincing. Berenblum,[1] from experimental work on mice, raised a warning in 1948, but there may still be differences between mice and men.

REFERENCE

1 Berenblum, I., *Brit. med. J.*, 1948, **2**, 601.

Fats for Lowering Serum Lipids

Q.—*In an unsaturated-fat diet for lowering serum lipids what is the relative efficacy of the following oils: soya, maize, safflower, and sunflower? What about olive oil?*

A.—Present data suggest that fats with iodine values over 100 are equally effective and produce the lowest cholesterol levels. Such fats are: soya, maize, safflower, and sunflower, and cotton seed oils. Olive oil with an iodine value of 90 is only rarely as effective as the more highly unsaturated oils.

Congenital Cataract

Q.—*A newborn baby has both lenses completely opaque from congenital cataract. What is the optimum age for needling of the cataracts, and should only one be done?*

A.—The surgical treatment of congenital cataract was discussed at a meeting of the Ophthalmological Society of the United Kingdom in 1957,[1] and the questioner is referred to this for a full consideration of the problems involved. In the case cited, my own opinion is that both eyes should be operated upon after the age of 6 months. Linear extraction with an iridectomy probably reduces the incidence of retinal detachment in later life, and is preferable to repeated needlings.

REFERENCE

1 Nutt, A. B., *Trans. ophthal. Soc. U.K.*, 1957, **77**, 39-57.

Exercises for Increasing Height

Q.—*Are there any exercises designed to increase height in adolescents before the epiphyses are fully united?*

A.—There are no exercises which will increase the height of adolescents, though they may appear taller if they are taught postural exercises.

Collected Articles from the "British Medical Journal"

The following books are available through booksellers or from the Publishing Manager, B.M.A. House. Prices, which include postage, are now the same for both inland and overseas.

Refresher Course for General Practitioners, Volume 3 (26s. 9d.).
Clinical Pathology in General Practice (22s. 3d.).
Any Questions?, Volume 3 (8s. 3d.).

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